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INFECTIVE HEPATITIS

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INTRODUCTION

For the last many years till 1942 the number of cases of catarrhal jaundice admitted into the King George Hospital was only very few about six to eight cases per year. During the years 1942 and 1943 the number became triple and in 1944 the disease was seen in an epidemic form. The paper is a summary of the observations made by the author from a study of 312 cases admitted during the course of the last ten years, from 1935 to 1944.

HISTORICAL

According to Rolleston and McNee (1929) the word jaundice is derived from the French word *jaune* meaning yellow. The word icterus is supposed to be derived from *iktis*, the yellow-breasted marten (Wickham Legg 1880), *iktepos*, the golden oriole or from *iktivos*, a kite.

The condition is known under different names such as, simple jaundice, catarrhal jaundice, infectious jaundice, acute hepatocholangitis, toxic hepatitis, and infective hepatitis. The epidemic in France is called as *junisse de champs* (Wilcox, 1919) and in Germany as *kriege icterus catarrhalis* or *soldaten krankheit icterus* (Buchbinder, 1920). Sporadic and epidemic forms of catarrhal jaundice have been known for centuries. Weil (1886) described a clinical condition of epidemic jaundice now known as Weil's disease and Quincke and Hoppe-Seyler (1898) definitely differentiated the two diseases. Cockayne (1912) proved that simple jaundice is infectious and essentially the same whether it occurs sporadically or in epidemics. Inado and Ido (1914) isolated *Leptospira icterohæmorrhagica* from cases of Weil's disease and definitely proved that the disease is different from epidemic catarrhal jaundice or infective hepatitis.

Epidemics of catarrhal jaundice have been observed and described by various observers from different parts of the world. Woodward (1875) from the United States reported one of the biggest epidemics that occurred during the civil war (1861-65). In the first year, there were 10,922 cases, second year 12,154 cases; third year 9,057 cases and in the fourth year 294 cases. Segall (1872) reported 2,344 cases in the Prussian army, 1,311 cases in the Bavarian army and 407 cases in the Saxon Army during the Franco-Prussian War (1870-71). Willcox (1916) reported 5,648 cases during the South African War. During the World War No. 1 (1914-18) there was an epidemic of catarrhal jaundice among the soldiers in the Middle East (Wilcox, 1919). Morgan and Brown (1927) described an epidemic in which 200 cases occurred in Midlands with one fatality. Booth and Okell (1927) described an epidemic from Surrey; Pickles (1930) from Yorkshire; Findlay *et al* (1931) from Surrey affecting school children; Glover and Wilson (1931) an extensive epidemic of catarrhal jaundice from public schools; Bashford (1934) an epidemic in workers of general post office, London; Montford (1934) in Leicestershire; Frazer (1935) among children in Staffordshire; Ramage (1935) an epidemic in Holland in school children; Lisney (1937) in school children; Sergent (1937) in school children at Gateshead-on-Tyne; Barber (1937) an epidemic in two institutions; Den Hartog (1937) from Holland; Deines (1938) from Germany; Pickles (1939) from rural districts in England; Maitland and Winner (1939) a small outbreak in the wards of a London Hospital; Cullinan (1939) epidemics in England from 1926; Bock (1939) from Switzerland; Norton (1939) from United States of America; Newman (1942) from the village of West Dean England; Cameron (1942) from soldiers in Palestine; Ian Gordon (1943) from the Middle East Forces; Ottenberg and Spigel (1943) from Mount Sinai Hospital, New York an epidemic that occurred in an Orphan Asylum; and Damodaran and Hartfall (1944) an epidemic from Malta. Lucke (1944) described in detail the postmortem appearances after a study of 125 autopsies from one of the severest epidemics that occurred in the United States in 1942.

AETIOLOGY

In all epidemics the source of infection could be traced to a patient suffering from infective hepatitis, but at what stage the patient is infective has not been definitely known. Newman (*loc. cit.*) states that the patient is infective very early in the disease and quotes the case of the headmaster of a school who was sick only for one day having infected four children while passing through the class room. The infection in these cases might be air-borne or droplet infection. Ottenberg and Spigel (1943) believe that infectivity ends with the appearance of jaundice. Pickles, Newman and others (*loc. cit.*) observed the transmission of the disease by persons sleeping together. In two of the cases of the present series the infection was from cases during the second or the third stage of the disease and that

too by sleeping together. In the third case an hour's contact with a patient during the second stage was sufficient for the transmission of the disease.

Voget (1942) succeeded in transmitting the disease to two of the four patients by oral administration of the duodenal juice. Successful transmission of the disease by the inoculation of blood or plasma have also been reported by Voget (*loc. cit.*) and Cameron (*loc. cit.*). Anderson (1937) succeeded in transmitting infective hepatitis from man to pigs. MacCallum and Bradley (1944) succeeded in transmitting infective hepatitis to patients suffering from rheumatoid arthritis by oral administration or by spraying the nasopharyngeal region with fæces or nasopharyngeal washings from patients in different stages of the disease.

Haven *et al* (1945) showed that the virus of infective hepatitis is present in the nasal secretions as well as in the fæces and succeeded in transmitting the disease to human volunteers by nasopharyngeal spray or by oral administration of the fæces in capsules. The oral administration of serum from cases of infective hepatitis in capsules has also resulted in the successful transmission of the disease after an incubation period of 28 days. The transmission experiments conducted by the author were negative.

The term infective hepatitis has also been applied to jaundice after yellow fever vaccination, injection of convalescent serum and arsenical injections. The first two are not included in this series and the third has been dealt with elsewhere in this paper. Post-arsenical jaundice has now been claimed to be due to and transmitted by improperly sterilized syringes (Salman *et al.*, 1944). Sheaham (1944) reported the occurrence of jaundice in laboratory attendants who were either helping in the arsenical injections or handling the infected syringes and test tubes.

The infective agent is in all probability a virus.

Pathology

Lucke (1944) described the changes that occur in the earlier stages of infective hepatitis from a study of specimens of liver of cases that got cured and died some time later, as a result of accident or some intercurrent disease. In two cases that died, one of acute alcoholism and another of intercurrent infection, regeneration of the liver cells were observed, in three cases that died within a month after recovery slight degenerative changes were observed, and in the remaining nine the regeneration was complete.

In cases that died of infective hepatitis the main changes were observed in the liver which was smaller, normal or bigger depending on the stage of the disease, smaller in the early stages and markedly enlarged during the chronic stage. Final shrinkage occurred in some cases before death. Naked eye appearance showed that the changes were not uniformly distributed but were patchy, red and yellow alternating. The red areas under microscope showed complete degeneration and the yellow areas hyperplasia, of the liver cells.

In Lucke's series 60 per cent of the cases had ascitis. Cases showing jaundice, low fever and ascitis have been separated from this group and will be published in another paper under the heading of toxic cirrhosis of liver.

A detailed study on pathology of infective hepatitis is being worked out in collaboration with Dr. T. Bhaskara Menon, Professor of Pathology will form the subject matter of a separate communication.

Incidence

1. *Age and Sex*—Table 1 gives the distribution of cases of infective hepatitis according to age and sex.

Table 1—Showing Distribution according to Age

Year.	0-5	6-10	11-15	16-20	21-25	26-30	31-35	36-40	41-45	Above 50	Total
1935	..	..	..	2	2	1	3	1	1	..	10
1936	..	..	..	1	2	2	1	2	..	..	8
1937	..	..	..	2	..	2	..	..	..	..	4
1938	..	..	..	2	1	2	2	1	1	..	9
1939	..	..	..	1	2	4	2	1	..	..	10
1940	..	..	..	..	1	2	..	1	..	..	4
1941	..	..	..	2	..	3	..	1	1	..	7
1942	..	..	..	12	6	7	2	..	1	..	28
1943	..	..	..	4	18	5	3	5	..	..	35
1944	3	..	1	45	80	40	15	3	3	7	197
	3	..	1	71	112	68	28	15	7	7	312

The minimum age was 4 and the maximum 60 years. The highest incidence was between 16 and 35 years thereby showing that the epidemic was one of young adults. Three cases occurred in children below 5 and seven cases in persons above 45 years of age.

Sex Incidence—Table 2 gives the incidence according to sex.

Table 2

Sex	*Number of Cases*
Males	304
Females	8
Total	312

The incidence in females is not so low as is represented by the above figures but there is a definite preponderance of the disease in males. The low incidence in children is a striking feature.

Distribution according to nationality—Table 3 shows the incidence according to nationality.

Table 3

		Males	*Females*	*Total*
1. Europeans and Anglo-Indians	..	9	2	11
2. Indians: (*a*) Hindus	..	235	5	240
(*b*) Muhammadans	..	37	0	37
(*c*) Indian Christians	..	23	1	24
Total	..	304	8	312

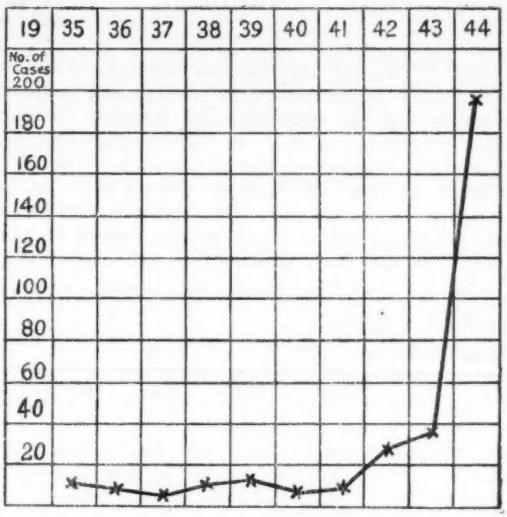


CHART 1—Showing incidence of disease: starting of the epidemic in 1942 and highest incidence in 1944.

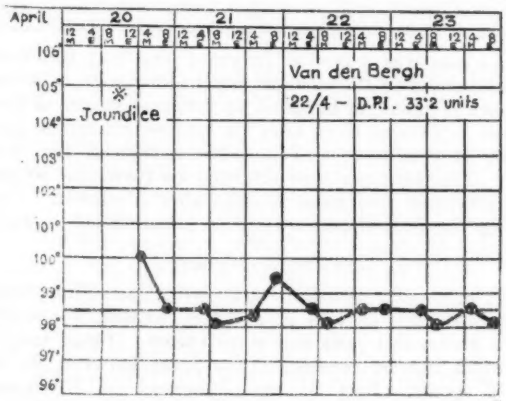


CHART 3—Four-hourly temperature chart showing mild fever varying between 99° and 101°·0F.

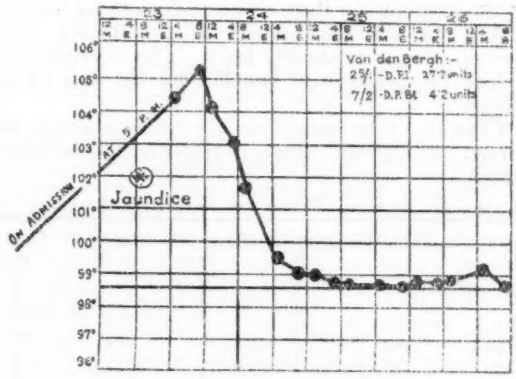


CHART 5—Four-hourly temperature chart showing the highest temperature 105°·4F. The temperature came down to normal in two days.

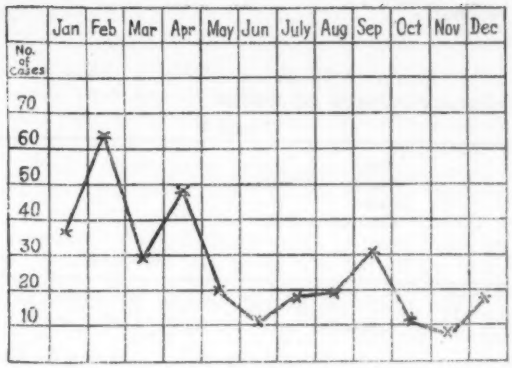


CHART 2—Showing seasonal variation. The maximum incidence is between the months of January to June.

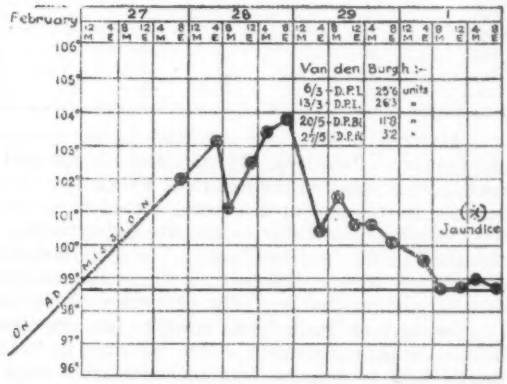


CHART 4—Four-hourly temperature chart of another patient (Case 15) which simulated influenza or dengue fever. Maximum temperature was 104°·0F.

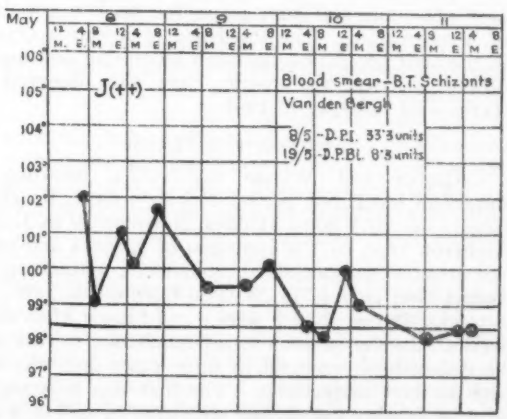


CHART 6—Four-hourly temperature chart of a patient suffering with infective hepatitis and benign tertian malaria. The patient had quinine in addition to the routine treatment of infective hepatitis.

Professional Incidence—Table 4 shows the incidence according to profession.

TABLE 4

1.	Doctors	3
2.	Medical students	3
3.	Nurses	3
4.	Nursing orderly	1
	Toatl ..	10

The incidence among medical personnel is very low when compared with the number of cases handled by them. Two of the medical students who had jaundice were in the preclinical course and evidently had nothing to do with cases of infective hepatitis admitted into the hospital. One of the house physicians attributed his jaundice to the taking of blood for Van den Bergh reaction from cases of infective hepatitis, but other house physicians who were similarly engaged in taking a larger number of specimens of blood at more frequent intervals from similar cases were not affected.

Seasonal Variation—Seasonal occurrence has been tabulated as follows:

TABLE 5—SHOWING SEASONAL VARIATION

Year	*Jan.*	*Feb.*	*March*	*April*	*May*	*June*	*July*	*Aug.*	*Sept.*	*Oct.*	*Nov.*	*Dec.*	*Total*
1935 ..	1	1	..	3	4	..	..	..	..	1	..	..	10
1936 ..	2	..	..	1	..	1	..	2	..	1	1	..	8
1937 ..	..	..	..	..	1	..	1	1	1	..	..	..	4
1938 ..	1	2	..	1	..	..	1	1	2	..	..	1	9
1939 ..	1	..	..	..	1	1	2	1	3	..	1	..	10
1940 ..	..	..	1	..	1	1	1	..	..	..	..	..	4
1941 ..	1	..	1	..	..	..	2	2	1	..	..	..	7
1942 ..	2	1	..	..	1	1	2	5	9	3	1	3	28
1943 ..	8	6	3	..	..	2	2	1	2	4	2	5	35
1944 ..	20	53	23	44	12	5	7	6	13	3	3	8	197
Total ..	36	63	28	49	20	11	18	19	31	12	8	17	312

Majority of the cases occurred during the months of January, February, March and April and the maximum number in the month of February. A slight increase in the number of cases occurred in September.

As shown in Table 6 infective hepatitis has been classified under four headings. The differentiation of these stages will be dealt with in the section of symptomatology of the disease. The first stage of the disease *i.e.,* the stage of "hæmolytic" jaundice was not observed before the commencement of the epidemic in 1942 and in the next two years 1943 and 1944 this stage was very often observed. It is possible that sporadic cases of infective hepatitis (catarrhal jaundice) in the first stage might have been mistaken for simple hepatitis especially when the cases got cured without proceeding on to the second stage.

The epidemic was first noticed amongst the military personnel and later on in the civilian population of Vizagapatam. The incidence of infective hepatitis in the civil population has been increasing and medical officers all over the district have also observed this increase of jaundice in 1944.

INCUBATION PERIOD

Glover and Wilson (*loc. cit.*) recorded the minimum incubation period of 3 to 4 days, Booth and Okell (*loc. cit.*) 20 to 41 days, Newman 29 to 31 days, Cameron (*loc. cit.*) a minimum of 32 days and one to six months in inoculated volunteers, Ottenberg and Spigel (*loc. cit.*) 17 to 28 days, Gordon (*loc. cit.*) 4 to 5 weeks, Barber 3 to 5 weeks and Lisney (*loc. cit.*) 4 weeks. In the present series incubation period could be definitely determined in three cases and was 4, 19 and 30 days respectively. The first was a young girl of 4 years who was playing with another girl of 4 years suffering from infective hepatitis in the second stage. Four days later the symptoms started with vomiting, loss of appetite and slight fever, urine was bile-stained the next day and jaundice appeared the day after. The second case was a boy of 18 years who was admitted for bronchitis in the medical ward along with a series of cases of infective hepatitis in different stages of the disease. Ninteen days later he noticed change in the colour of the urine and jaundice developed the day after. The third case was admitted for rheumatic joints and developed symptoms 30 days after admissoin. The average incubation period may be taken as one month.

SYMPTOMATOLOGY

The disease usually starts with gastro-intestinal symptoms such as loss of appetite, nausea, vomiting, slight abdominal pain and constipation. Fever might or might not be present. Low fever between 99 to 101°F (*vide* Chart 3) was observed in 27 cases. Still higher or medium rise of temperature, 101 to 102°F, was observed in 14 cases. High rise of temperature, above 103°F (*vide* Chart 5) was observed in seven cases. These high temperatures generally last only for three or four days and are usually mistaken for the short fevers of the tropics, *viz.,* influenza, dengue or sandfly fever. The injected eyes will hide the presence of jaundice for the first 24 to 48 hours.

Clinically four stages of the disease could be observed during the present epidemic of infective hepatitis.

TABLE 6—SHOWING STAGES OF INFECTIVE HEPATITIS

	Stage I	*Stage II*	*Stage III*	*Stage IV*	*Total*
1935	1	9	..		10
1936	2	6	..		8
1937	1	3	..		4
1938	3	6	..		9
1939	4	6	..		10
1940	1	3	..		4
1941 .. 1	2	4	..		7
1942 .. 3	5	20	..		28
1943 .. 2	9	23	1		35
1944 .. 9	90	97	1		197
Total .. 15	118	177	2		312

1. *First Stage*—The stage of "hæmolytic" jaundice.

2. *Second Stage*—The stage of toxic and infective hepatic jaundice.

3. *Third Stage*—The stage of obstructive hepatic jaundice.

4. *Fourth Stage*—The terminal stage.

The Stage of "Hæmolytic" Jaundice—Jaundice was observed clinically in all the fifteen (4·8 per cent) cases of the first stage. The liver was enlarged, palpable and tender in all the cases. Bile was absent from the urine in all, motions contained bile, and Van den Bergh reaction showed "hæmolytic" jaundice, the quantity of bilirubin varied from traces insufficient for quantitative estimation to 5·2 units. In four cases Van den Bergh showed direct positive delayed and varying from 2·4 to 4·8 units. A second examination done at the end of a week showed traces of bilirubin quite insufficient for quantitative estimation. In very mild cases icteric tinge of the conjunctivæ might not be observed for the first two or three days but if the blood is examined for bilirubin, indirect Van den Bergh reaction will be positive.

All except one came for admission before the first week and seven of this before the third day. Their stay in the hospital varied from 6 to 18 days, the average duration being 10 days. In all the cases the infection has been very mild and they came for observation very early. Prompt recognition of the condition, strict restriction of diet and saline purgatives prevented the condition going on to the second stage or the stage of toxic and infective jaundice. The duration of the disease varied from 10 to 20 days and the average 15 days.

A brief summary of two cases are given below:—

Case 1—Mohammadan male, aged 22 years, was admitted on 12-4-44, with a history of abdominal pain and vomiting of a day's duration. *Examination* showed slight jaundice and a just palpable and tender liver. Urine did not show any bile, motions contained bile and Van den Bergh reaction was direct positive delayed. Total bilirubin 1·8 units. He was discharged cured after eight days stay in the hospital.

Case 2—Hindu male, aged 22 years, was admitted on 11-3-44 with a history of indigestion and abdominal pain of three days duration. *Physical examination* showed jaundice and a palpable and tender liver. Urine showed no bile, motions contained bile. Van den Bergh on 14-3-44 was direct positive delayed and total bilirubin 2·4 units. At the end of a week the jaundice improved and Van den Bergh on 21-3-44 showed a direct positive delayed reaction, quantity too small for estimation. The patient was discharged cured after eleven days stay in the hospital.

The Stage of Toxic and Infective Hepatic Jaundice—One hundred and eighteen (37·8 per cent) cases belonged to this group. Symptoms were more marked than in the first stage. Fever was a more constant feature, nausea and vomiting were pronounced, deep or greenish colouration of the urine has been observed in many; and jaundice a few days before, simultaneously, or a few days after the appearance of bile in the urine. Liver was enlarged and tender in all the cases. Although some of the patients complained of very severe colicky pains in the abdomen, the areas of tenderness was located only to the area of the liver. Yellow colouration of the body was present only in five cases and the bilirubin content of these cases was high. Pruritus was not present in any of the cases. Constipation was the rule. Urine and motions showed bile in all the cases, and Van den Bergh reaction showed direct positive biphasic reaction, total bilirubin varying from 3 to 45 units. The transition from the hæmolytic to the toxic and infective stage could not be observed since the patients were admitted only a few days later. During the process of recovery the jaundice gradually lessened and before the blood returned to normal, the Van den Bergh reaction passed from direct positive biphasic (toxic and infective jaundice) to direct delayed or indirect positive ("hæmolytic" jaundice). The patients remained in the hospital from 15 to 45 days. The average duration of the disease varied from three to six weeks.

A brief summary of five cases is given below:—

Case 3—Hindu male, aged 25 years, was admitted on 17-12-43 with a history of jaundice, loss of appetite and passing of green coloured urine of ten days duration. *Physical examination* showed jaundice and an enlarged and tender liver. Urine showed bile salts and pigments. Motions contained bile. Van den Bergh on 20-12-43 showed direct positive biphasic reaction, total bilirubin 8·9 units. The patient gradually became better. Van den Bergh on 27-12-43 showed direct positive biphasic reaction, total bilirubin 3·0 units and on 3-1-44 direct positive delayed reaction, total bilirubin 2·6 units. He was discharged cured after a stay of 18 days in the hospital.

Case 4—Hindu male, aged 35 years, was admitted on 26-12-42 with a history of indigestion, abdominal pain and vomiting of seven days duration. *Physical examination* showed jaundice and an enlarged and tender liver. Urine contained bile salts and bile pigments, motions contained bile and Van den Bergh on 27-12-42 showed direct positive biphasic reaction, total bilirubin 8·8 units. He was put on a restricted diet, alkalies by mouth and saline purgatives daily for the first week and later every alternate day. The patient gradually improved, jaundice disappeared, liver became normal in size and Van den Bergh reaction on 8-1-44 showed a direct positive delayed reaction, total bilirubin 0·9 units. He was discharged cured after a stay of 14 days in the hospital.

Case 5—European male, aged 24 years, was admitted on 12-10-43 with a history of indigestion, vomiting, low fever, and yellow colouration of the conjunctivæ of one week's duration. *Physical examination* showed jaundice of a moderate intensity, and a palpable and tender liver. Urine contained bile salts and pigments, and motions contained bile. Van den Bergh on 13-10-43 showed direct positive biphasic reaction, total bilirubin 20·9 units. The patient gradually became better and Van den Bergh on 1-11-43

showed direct positive delayed reaction, total bilirubin 0·9 units. He was discharged cured after a stay of 33 days in the hospital.

Case 6—Indian Christian, male, aged 19 years, was admitted on 5-12-43 with a history of indigestion and jaundice of ten days, and passing green coloured urine of four days duration. *Physical examination* showed well developed jaundice and definitely enlarged and tender liver. Urine contained bile salts and pigments. Motions contained bile. Van den Bergh reaction taken on different occasions are given below:—

		Total bilirubin
6-12-43:	Direct positive biphasic.	45·9 units
13-12-43	do.	19·2 „
20-12-43	do.	8·9 „
27-12-43	do.	4·9 „
3- 1-44	do.	3·3 „

This case showed the highest figure for direct positive biphasic reaction. The patient was discharged cured after a stay of 30 days in the hospital.

Case 7—An atypical case with low bilirubin content.—Hindu male aged 22 years was admitted on 22-6-44 with a history of slight fever, indigestion and vomiting of two days' duration. *Physical examination* showed mild jaundice and a slightly palpable and tender liver. Temperature 102·0F and pulse 100 per minute. Blood smear showed no parasite and the leucocytic picture was normal. Bile was present in the motion but absent in urine. Van den Bergh reaction on 12-6-44 showed direct positive biphasic, total bilirubin 2·8 units. A second examination five days later showed direct positive delayed, total bilirubin 2·4 units. He gradually improved and was discharged after a stay of ten days in the hospital. He reported sick again on 26-7-44 with the same symptoms as before. Jaundice was slight, urine was acholic and Van den Bergh reaction on 26-7-44 showed direct positive biphasic, total bilirubin 3·7 units. The patient gradually improved by restriction of diet and intravenous glucose. Van den Bergh on 7-8-44 showed direct positive delayed, total bilirubin 1·9 units. Blood cholesterol on 26-7-44 showed 177·4 mg. and ten days later 127 mg. per 100 c.c. showing a definite reduction after treatment.

The Stage of Obstructive Hepatic Jaundice—One hundred and seventy seven (56·7per cent) cases belonged to this group. The symptoms were much more advanced than in the second stage; fever was present more often. Abdominal discomfort nausea and vomiting were constant features. Jaundice was more pronounced than in the second stage. Bile was present in the urine but was absent from the motions only in a few cases. Daily examination of faeces could have revealed larger number of cases showing the absence of bile from the motions. Yellow colouration of the body was present in 15 cases and pruritus in 26 cases, slight in 16 and severe in 10. Abdominal pain was observed more often. In one case it simulated renal colic and in another the pain was so severe that the patient wanted to commit suicide, but was discharged cured with injections of calcium gluconate. Van den Bergh reactions showed direct positive immediate, the total quantity of bilirubin varying from 8 to 62 units, the average being 25 units. In a few cases the jaundice was toxic and infective at the beginning and later became obstructive. During the process of recovery, obstructive hepatic jaundice became toxic and infective and finallly hæmolytic. In some cases (No. 11) irregularities in diet were responsible for the increase in the jaundice and further restrictions of the diet completely cured the patients. Hæmorrhage was present in 3 cases, epistaxis in two and bleeding from the rectum in the third. Herpes labialis was present in one case and spider angioma of the nose in another case. Majority of the patients were admitted into the hospital during the first ten days, few within a fortnight and 3 cases after a month. The average duration of the stay in the hospital was four to six weeks. Two patients remained in the hospital for more than sixty days and in both the cases it was due to indiscretion in diet while in hospital.

A brief summary of eight cases are given below:—

Case 8—Hindu male, aged 22 years, was admitted on 15-1-42 with a history of indigestion, slight fever and constipation of ten days' and green colouration of the urine and jaundice of three days' duration. He takes alcohol occasionally. *Physical examination* showed fairly well developed jaundice and an enlarged and tender liver. Both urine and motions contained bile. The results of the Van den Bergh reaction taken on various occasions are as follows:

		Total bilirubin
20-1-42	Direct positive immediate.	22·73 units
26-1-42	do.	14·10 „
2-2-42	do.	7·10 „
10-2-42	Direct positive delayed.	1·80 „

The patient gradually improved, liver became normal in size and bile disappeared from the urine. The patient was discharged cured after a stay of 31 days in the hospital.

Case 9—Muhammadan male, aged 35 years, was admitted on 16-3-43 with a history of constipation and indigestion of 12 days; and passing green coloured urine and yellow colouration of the conjunctivæ of 8 days' duration. *Physical examination* showed a definitely enlarged and tender liver, just palpable spleen, fairly well-developed jaundice and yellow colouration of the body. Urine showed bile salts and bile pigments but the motions were acholic. Results of Van den Bergh reaction done on successive occasions are given below:

		Total bilirubin
17-3-43	Direct positive immediate	50·2 units
27-3-43	do.	36·4 „
3-4-43	Direct positive biphasic	13·2 „
13-4-43	Direct positive delayed	7·35 „
20-4-43	do.	6·90 „
3-5-43	do.	1·90 „

The patient gradually improved by the routine method of treatment and was discharged cured after a stay of 49 days in the hospital, the total duration of the disease being 61 days.

Case 10—Indian Christian, male, aged 24 years, was admitted on 23-1-43 with a history of low fever and loss of appetite of 11 days' duration, and jaundice and green colouration of the urine of one week's

duration. *Physical examination* showed deep jaundice, a just palpable spleen and a definitely enlarged and tender liver. Urine showed bile salts and bile pigments, and motions pale in colour due to traces of bile pigments. Low fever was present for the first three days while in the hospital. Pulse was slow (56 per minute) Van den Bergh reaction done on successive occasions showed the following results:

		Total bilirubin
2-2-43	Direct positive immediate	62·0 units
9-2-43	do.	40·0 ,,
15-2-43	Direct positive biphasic	11·1 ,,
22-2-43	do.	5·9 ,,
1-3-43	do.	3·0 ,,

As a result of routine treatment the patient gradually improved. Motions became normal in colour and bile disappeared from the urine. The patient was discharged cured after a stay of 47 days in hospital, the total duration of the disease being 58 days.

Case 11—Gradual recovery and then relapse due to irregularity in diet—Hindu male, aged 20 years, was admitted on 8-3-44 with a history of constipation, indigestion, yellow colouration of the eyes and passing green coloured urine of five days' duration. Physical examination showed well developed jaundice and an enlarged and tender liver. Urine and motions contained bile. Van den Bergh reaction done on different occasions showed the following results:

		Total bilirubin
9-3-44	Direct positive immediate	32·7 units
15-3-44	Direct positive biphasic	13·9 ,,
22-3-44	do.	10·0 ,,
	(The patient was given a liberal diet and the jaundice deepened)	
3-4-44	Direct positive immediate	52·6 ,,
8-4-44	do.	48·0 ,,
12-4-44	do.	41·4 ,,

During the first two weeks' stay in the hospital with restricted diet, saline purgatives and alkalies by mouth the patient showed definite improvement. The liver became smaller in size and the jaundice changed from the obstructive hepatic to toxic and infective type. A few days indiscretion in diet produced deepening of the jaundice and reversion from the toxic and infective to the obstructive hepatic type. Restriction of diet and routine treatment showed definite improvement and he was discharged on 26-4-44 (fourteen days after the last Van den Bergh) after a stay of 49 days in the hospital.

Case 12—Jaundice increased in intensity changing from toxic and infective to obstructive hepatic jaundice, the condition was then reversed and the patient was discharged cured.—Indian Christian, male, aged 29 years, was admitted on 17-1-44 with a history of low fever, constipation and vague abdominal pains of 12 days' and jaundice and green colouration of the urine of 8 days' duration. *Physical examination* showed jaundice, a just palpable spleen and an enlarged and tender liver. Urine contained bile salts and bile pigments and motion was bile stained. Van den Bergh reaction showed the following results:

		Total bilirubin
25-1-44	Direct positive biphasic	23·5 units
1-2-44	Direct positive immediate	43·3 ,,
7-2-44	do.	16·7 ,,
14-2-44	Direct positive biphasic	6·6 ,,

The persistent vomiting and abdominal pain was clinically indicative that the jaundice was deepening and this observation was confirmed by Van den Bergh reaction. In addition to the routine treatment he was given intravenous calcium gluconate daily and intramuscular injections of vitamin K twice a week. This caused rapid improvement of the symptoms and the jaundice gradually disappeared. The patient was discharged practically cured after a stay of 29 days in the hospital, the total duration being 41 days.

Case 13—Sudden onset and gradual improvement of jaundice, controlled by Van den Bergh reaction for seven consecutive weeks.—Indian Christian, male, aged 22 years, was admitted on 30-11-43 with a history of fever, loss of appetite, yellow colouration of the conjunctivæ and passing green coloured urine of eight days duration. *Physical examination* showed fairly well developed jaundice and an enlarged and tender liver. Urine showed bile salts and bile pigments and motions contained bile. The gradual improvement of jaundice is shown by the Van den Bergh reaction:

		Total bilirubin
1-12-43	Direct positive immediate	40·0 units
6-12-43	do.	33·3 ,,
13-12-43	Direct positive biphasic	35·7 ,,
20-12-43	do.	13·5 ,,
27-12-43	do.	12·1 ,,
3-1-44	do.	4·9 ,,
10-1-44	Direct positive delayed	2·9 ,,

The patient was discharged cured after a stay of 46 days in the hospital, total duration of the disease being 54 days.

Case 14—Low bilirubin content in obstructive hepatic jaundice.—Hindu, male, aged 19 years, was admitted on 14-2-44 with a history of low fever, loss of appetite and vomiting of 10 days' and jaundice of four days' duration. *Physical examination* showed jaundice and a slightly enlarged and tender liver. Urine showed bile salts and bile pigments, and motions contained bile. Van den Bergh reaction on 22-2-44 showed direct positive immediate, total bilirubin 7·8 units. The patient gradually improved and Van den Bergh on 2-3-44 showed direct positive biphasic, total bilirubin 5·1 units. He was discharged cured after a stay of 18 days in the hospital.

Case 15—Onset with high fever of 104°F. slight increase in jaundice first and later gradual recovery.—Hindu, male, aged 22 years, was admitted on 27-2-44 with a history of fever, very severe headache burning sensation in the eyes and vague abdominal pains of a day's duration. *Physical examination* showed flushed face, injected eyes and slight increase in the pulse (100 per minute) and respirations (24 per minute). All the systems were normal. Liver was not enlarged. Blood smear showed no parasites but only leucopenia. Urine showed phosphates, but bile salts and bile pigments were absent. The clinical picture looked like that of influenza or dengue fever, and the temperature (*vide* Chart 4) came to normal on 1-3-44. The same day the patient noticed change in the colour of the urine to greenish yellow (bile stained). On 3-3-44 definite jaundice was observed and examination of the urine showed bile salts and bile pigments. After the

fall of the temperature the pulse and respirations came to normal. The day after, liver was definitely palpable and tender but spleen was not enlarged. Nausea and vomiting continued and the jaundice increased. Van den Bergh reaction done on successive occasions showed the following results:

		Total bilirubbin
6-3-44	Direct positive immediate	25·6 units
3-3-44	do.	26·3 „
20-3-44	Direct positive biphasic	11·2 „
27-3-44	do.	3·2 „

The patient was put on a restricted diet, mag sulph and alkalies by mouth and calcium gluconate intravenously. He had an uneventful recovery and was discharged cured after a stay of 30 days in the hospital.

In this case the injection of the eyes prevented the recognition of the jaundice earlier, and the presence of bile in the urine gave a clue as to the correct diagnosis.

Case 16—Increase in intensity of jaundice and gradual recovery.—Hindu, male, aged 20 years, was admitted on 24-10-42 with a history of indigestion, vague abdominal pains, vomiting and jaundice of 16 days' duration. *Physical examination* showed jaundice, just palpable spleen and an enlarged and tender liver. Urine showed bile salts and bile pigments, motions did not contain any bile and Van den Bergh reaction done on successive occasions showed the following results:

		Total bilirubin
27-10-42	Direct positive immediate	25·2 units
13-11-42	do.	57·2 „
28-12-42	Direct positive biphasic	5·6 „

Pulse remained slow at the rate of 58 per minute during the height of the disease. The patient gradually improved after the routine treatment and was discharged cured after a stay of 69 days in the hospital.

The Terminal Stage

The signs and symptoms of this stage were the same as of the previous stage but more advanced. The main feature was the enlargement of the liver which in one case reached an inch above the level of the umbilicus. The jaundice was obstructive hepatic and in both the cases the bilirubin content was decreasing after a few days, but the general condition of the patient gradually became worse, the coma became deeper and the patient finally died.

Only two cases were observed in the fourth or the terminal stage and a summary of these cases are given below:—

Case 17—Hindu, male, aged 35 years, was admitted on 12-10-43 with a history of jaundice of two months' duration. The disease was accompanied with fever during the first four days and was treated in another hospital prior to admission with six intravenous injections of calcium gluconate. *Physical examination* showed deep jaundice and a markedly enlarged and tender liver. Spleen was not enlarged and nothing abnormal could be detected in any of the other systems. Urine showed bile salts and bile pigments, and motions contained bile. Van den Bergh reaction taken on different occasions showed the following results:

		Total bilirubin
13-10-43	Direct positive immediate	26·3 units
26-10-43	do.	57·1 „
5-11-43	do.	57·1 „
13-11-43	do.	53·1 „
20-11-43	do.	41·7 „
26-11-43	do.	36·9 „
7-12-43	Direct positive biphasic	21·3 „

The patient was running a low fever between 99 and 101°F while in hospital. During the first week the jaundice became deeper and then it gradually diminished, but the reduction was not marked. The liver gradually became bigger in spite of the decrease in the jaundice. He had calcium gluconate intravenously and liver extract intramuscularly. From 2-11-43 he had insulin in addition for a week. On 30-11-43 he had an attack of hæmoptysis and was given injections of vitamin K in addition. The patient gradually became worse, went on to coma and finally died on 8-12-43. Postmortem was not available.

Case 18—Hindu, male, aged 31 years, was admitted on 10-3-44 with a history of indigestion, low fever and jaundice of 10 days' duration. *Physical examination* showed deep jaundice and a definitely palpable and tender liver. Other systems were normal. Van den Bergh reaction done on successive occasions showed the following results:

		Total bilirubin
13-3-44	Direct positive immediate	20·0 units
3-4-44	do.	44·4 „
8-4-44	do.	52·0 „
27-4-44	do.	40·6 „

Urine showed bile salts and bile pigments, motions did not contain any bile. For the first few days he had the routine treatment. After that, he had intravenous calcium gluconate in addition. The condition of the patient instead of showing improvement showed increasing intensity and the liver became still further enlarged. From 27-4-44 he was given 5 units of insulin in addition to intravenous calcium gluconate. Bile was absent from the motions only on two occasions and that too lasting only for 48 hours. On 2-5-44 the temperature rose up to 102·0F. Blood smear showed slight leucocytosis but no parasites. The same treatment was continued. Blood Wassermann was negative. Intramuscular injections of vitamin K were given in addition. The patient gradually became worse, coma became deeper and the patient died on 5-5-44. Postmortem was not available.

Circulatory System

Mitral stenosis was present in one, and mitral stenosis and aortic regurgitation in another case and in both the cases the jaundice was in second or toxic and infective hepatic stage.

Blood pressure varied from 88 to 130 mm. systolic and 30 to 86 mm. diastolic. The average blood pressure was low, 108 systolic and 70 diastolic. The minimum pressure was observed in a male aged 38 years in the third stage of the disease and was 88/40. In the case associated with mitral stenosis and aortic regurgitation the pressure was 100/30.

Bradycardia was observed only at the end of the second or in the third stage. The minimum pulse rate was 48 per minute. The irritability of the heart was tested in a few cases and the results are as follows:

Age	*Stage*	*Date*	*Lying down*	*Standing*
26	III		48	76
30	III		60	68
22	III	29/9	59	94
		4/10	55	106
30	III	29/9	61	114
		3/10	64	120
24	II	1/10	70	83
		3/10	80	94

Although the pulse rate was slow the increase in the rate was not much different from the normal. In the last case of mitral stenosis and aortic regurgitation the increase was only 13 at the first instance and 14 at the second, less than what was expected.

Electrocardiogram was taken in 2 cases (not included in this series) and showed nothing definitely abnormal.

Gastric Analysis

Seven cases were investigated. In one case the test was done at the termination of the attack (direct positive biphasic 1·6 units) and in all the other cases it was done at the height of the disease (Stage III). The following are the results:

Resting Juice—(1) Total quantity varied between 12 and 43 c.c.

(2) Total acidity varied from 16 to 68 c.c. Two cases showed decided increase, one 57 and the other 68 c.c. of N/10 HCl.

(3) Free HCl followed the same course as that of total acidity.

(4) Bile was present in five of the seven cases and in two of these in large quantities.

(5) Blood and mucus were absent in all.

Emptying time—The time varied between ¾ to 1½ hours *i.e.,* within normal limits.

Bile—Bile was present in one specimen in 1 case, in two specimens in 2 cases, in three specimens in 1 case and in all the 5 specimens in another.

Blood and mucus were absent in all the specimens.

Conclusion—One case showed slightly diminished acidity with rapid emptying of the stomach, four cases showed a tendency to hyperacidity and one case increased acidity suggestive of duodenal ulcer. One case showed normal curve. Bile was present in appreciable quantity in four cases and in one case it was present in all the specimens except in the quarter hour specimen.

Blood Examination

The condition of the blood was investigated in 34 cases:

1. The total R.B.C. count varied from 3·5 to 5·5 million and only two cases showed anæmia.

2. The total while cell count varied from 3000 to 10,500. Leucopenia was more often present, but leucocytosis was present only in a few cases. Differential count did not show any definite feature. Result was as follows:

	Polymorphs	*Lymphocytes*	*Mononuclears*	*Eosinophils*	*Basophils*
	%	%	%	%	%
1.	62	28	6	4	..
2.	74	15	6	4	1
3.	57	21	3	15	4
4.	78	20	2	..	..

3. Fragility of R.B.C. was normal in all the cases except in one case where it commenced at 0·65 per cent saline and was complete at 0·3 per cent saline. The blood was taken during the third stage but unfortunately a second examination was not done. Excess of oxalate in the blood specimen might be the cause of increase in the fragility of R.B.C.

In one case (Stage III) the fragility was estimated on three occasions and was found to be the same.

Date	*Fragility commenced at*	*Haemolysis complete at*
7/1	0·35% saline	0·20% saline
12/1	0·40% „	0·25% „
17/1	0·35% „	0·20% „

Blood Chemistry

1. Blood urea was normal in the cases investigated.

2. Blood calcium was normal in the cases investigated.

3. Blood cholesterol: Cholesterol varied from 65 to 177 mg. per 100 c.c. In two cases a second estimation was done at the end of a week, one case showed an increase from 65 to 112 and the second a decrease from 177 to 127 mg. per 100 c.c.

4. Lævulose tolerance test. This test was done only in one case and the findings are as follows:

Time.	*Blood sugar*	*Urine sugar*
Before laevulose	103·1 mg.	Nil
½ hr. after 30 gm of laevulose.	117·0 „	Trace
1 hr. do.	130·7 „	Present
1½ hrs. do.	129·0 „	„
2 hrs. do.	137·0 „	„

The test was done during the third stage and showed slight damage to the liver.

5. Hippuric acid test was done in one case and that showed normal liver function during the second stage of infective hepatitis.

Urinary Diastase

The diastase content of the urine was examined in four cases and was found to be within normal limits.

Blood Wassermann Reaction

Blood of 14 cases was examined for Wassermann reaction and one showed a strong positive (++) six moderate positive (+) and the rest negative reaction.

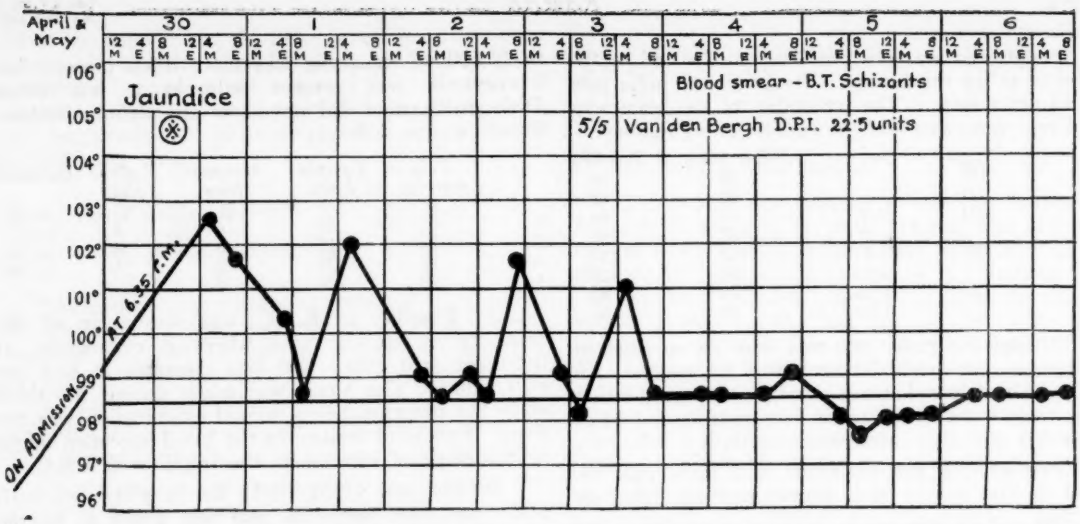


CHART 7—Four-hourly temperature chart of a patient (Case 19) with infective hepatitis and B.T. malaria. He was treated with quinine in addition to the routine treatment for infective hepatitis.

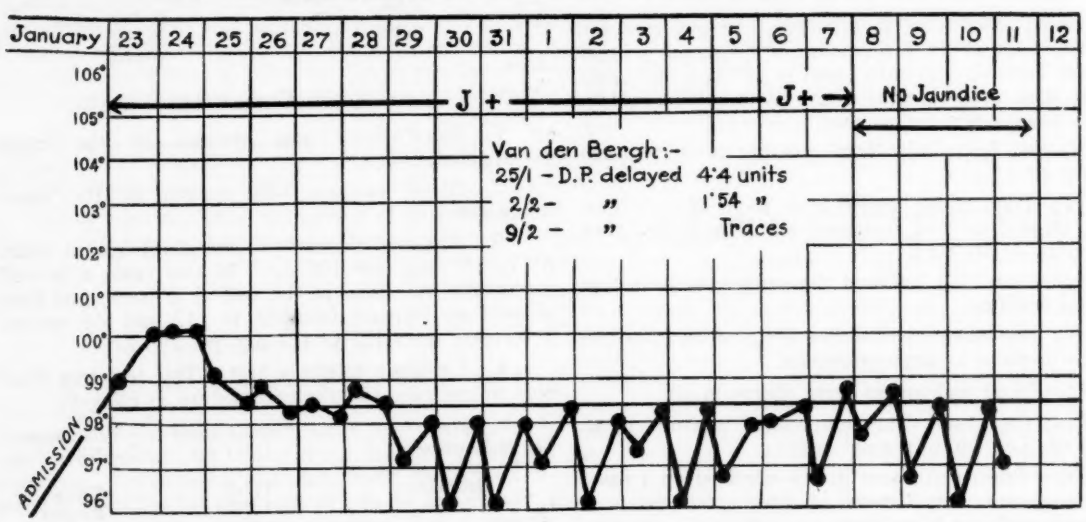


CHART 8—B.D. chart of a patient with infective hepatitis showing subnormal temperature occurring after the disease is cured. This condition has been observed in a few other cases also.

INFECTIVE HEPATITIS IN ASSOCIATION WITH OTHER DISEASES

The following diseases were observed with infective hepatitis:

		Number of cases
1.	Beri beri	1
2.	Malaria (Benign Tertian)	3
3.	Amoebic dysentery	2
4.	Bacillary dysentery	2
5.	Chronic bronchitis	1
6.	Fibrosis of lung	1
7.	Abscess	2
8.	Fracture of the femur	1
9.	Bleeding piles	1
10.	Pregnancy	1
11.	Mitral stenosis	1
12.	Mitral stenosis and aortic regurgitation	1

Brief summary of the cases associated with malaria, dysentery and pregnancy are given below:

Malaria: (Case 19)—Mohammadan, male, aged 24 years, was admitted on 30-4-44 with a history of fever and jaundice of 3 days' duration. *Physical examination* showed moderately developed jaundice, slightly palpable spleen and a palpable and tender liver. Blood smear showed rings and growing trophozoites of Plasmodium vivax, with Schuffner's dots. Urine contained bile salts and bile pigment and motions contained bile. Van den Bergh reaction on 5-5-44 showed direct positive immediate, total bilirubin 22·5 units. The patient was given the routine treatment for the jaundice, and in addition a single injection of quinine acid hydrochloride (5 grs. intramuscularly) and 5 grs. of quinine

sulph. a day by mouth for a week. The temperature came down to normal after four days (*vide* Chart 7) but the jaundice continued and the patient was discharged cured after a stay of 12 days in the hospital.

Case 20—Hindu, male, aged 24 years was admitted on 11-4-44 with a history of indigestion, low fever and jaundice of six days' duration. *Physical examination* showed moderately developed jaundice, enlarged spleen and liver and a temperature of 103·0F. Blood smear showed all stages of Plasmodium vivax. Urine showed bile salts and pigments, and motions contained bile. Van den Bergh reaction done on successive occasions showed the following results:

		Total bilirubin
12-4-44	Direct positive immediate	40·6 units
28-4-44	Direct positive biphasic	8·3 ,,
3-5-44	do.	2·8 ,,

The patient was put on Quinine (5 grs. a day) for one week in addition to the routine treatment for infective hepatitis. He was discharged cured after a stay of 25 days in the hospital.

In the third case the jaundice was well developed, both spleen and liver were enlarged, urine showed bile salts and bile pigments motions contained bile, and Van den Bergh reaction showed direct positive immediate, total bilirubin 33·3 units. Blood smear showed growing trophozoites and schizonts of Plasmodium vivax. The patient had 5 grs. of quinine sulph. a day by mouth for a week in addition to the routine treatment for infective hepatitis. A second Van den Bergh done 10 days later showed direct positive biphasic, total bilirubin 8·3 units. The patient was discharged cured after a stay of 17 days in hospital.

The three cases described above show that malaria is a co-existant condition. Jaundice is observed in malaria but not to the extent seen in these cases. In some cases of malaria, the jaundice might become toxic and infective hepatic but never obstructive hepatic. In addition to the routine treatment of infective hepatitis quinine has to be given. All the cases were infections with benign tertian (Plasmodium vivax).

Amœbic dysentery: (Case 21)—Hindu, male, aged 35 years, was admitted on 4-9-44 with a history of low fever and jaundice of one week's duration. *Physical examination* showed fairly developed jaundice and an enlarged and tender liver. Urine showed bile salts and pigments. Motions showed blood and mucus—picture of acute amœbic dysentery and under the microscope showed vegetative entamœba histolytica with ingested R.B.C. Van den Bergh reaction taken on successive occasions showed the following results:

		Total bilirubin
12-9-44	Direct positive immediate	21·7 units
18-9-44	Direct positive biphasic	9·6 ,,
25-9-44	Direct positive delayed	2·2 ,,

In addition to the routine treatment for infective hepatitis he had intravenous calcium gluconate and subcutaneous emetine injections. Gastric analysis showed hypermotility. He was discharged cured after a stay of 21 days in the hospital.

In the second case also motions showed actively motile E. histolytica with ingested R.B.C. Urine showed traces of bile pigments, and Van den Bergh reaction direct positive biphasic, total bilirubin 4·8 units. The patient was given emetine injections in addition to the routine treatment. A second Van den Bergh after ten days showed direct positive delayed, total bilirubin 1·1 units.

Bacillary dysentery—Of the two cases, one patient was admitted with symptoms of infective hepatitis and a few days later he developed acute bacillary dysentery. The dysentery was cured but the jaundice still persisted. Van den Bergh reaction showed direct positive immediate, total bilirubin 20 units. He was discharged cured after a stay of 13 days in the hospital.

Case 22—Hindu, male, aged 40 years, was admitted on 27-9-44 with a history of jaundice of 15 days duration. *Physical examination* showed deep jaundice and an enlarged and tender liver. Urine and motion contained bile. Van den Bergh reaction on 28-9-44 showed direct positive immediate, total bilirubin 11·9 units. Three days later the patient developed acute bacillary dysentery and had treatment for the same in addition. He was progressing favourably but pneumonic symptoms developed on 6-10-44 and the patient died two days later.

Postmortem showed yellow discolouration and slight degenerative changes in the liver, dysenteric (bacillary) ulceration of the colon and pneumonic consolidation of the right lower lobe. Detailed description will be given in a separate communication.

Pregnancy: (Case 23)—Hindu, female, aged 15 years was admitted on 6-6-44 with a history of vomiting, indigestion, loss of appetite and jaundice of four days' duration. She was in the sixth month of pregnancy at the time of admission. *Physical examination* showed fairly well developed jaundice and an enlarged and tender liver. The height of the uterus showed 22nd week of pregnancy and fœtal heart was clearly heard. Urine showed bile salts and pigments, and motions contained bile. Van den Bergh reaction done on successive occasions showed the following results:

		Total bilirubin
7-6-44	Direct positive immediate	35·7 units
17-6-44	Direct positive biphasic	15·1 ,,
26-6-44	do.	7·1 ,,
2-7-44	do.	4·0 ,,

She had intravenous calcium gluconate in addition to the routine treatment for infective hepatitis. She was discharged cured after a stay of 29 days in the hospital, and had a healthy baby at full term. The delivery was normal without any complications.

Relapses

Gordon (1943) *loc. cit.* noted relapses in 5 of the 168 cases in the Middle East. In the present series four cases were readmitted for varying symptoms out of which one was a true relapse.

Case 24—S. B. Hindu, male, aged 25 years, was admitted on 26-9-44. He had typhoid fever in 1942. His blood Wassermann was strong positive four months ago for which he had a course of arsenical injections. The present complaint started with jaundice, low fever and pain in the abdomen 15 days ago. *Physical examination* showed a moderately nourished individual with

jaundice, just palpable liver and spleen. Urine showed bile salts and bile pigments, motions contained bile; Van den Bergh reaction on 30-9-44; direct positive immediate; total bilirubin 12·8 units and on 9-10-44: direct positive delayed, total bilirubin 1·9 units. On 20-10-44: direct positive delayed, colour not sufficient for estimation. Patient was given the usual treatment and was discharged cured on 21-10-44 after a stay of 26 days in hospital.

He was readmitted on 24-1-45 for vague abdominal pain and fever 102·0F, which came down to normal the next day. He had dyspeptic symptoms which persisted. Van den Bergh reaction showed direct positive delayed; colour insufficient for estimation. He was discharged cured on 3-2-45.

Patient was admitted a third time on 22-2-45 with recurrence of jaundice, vague abdominal pains and loss of appetite. *Physical examination* showed a just palpable liver and spleen, urine showed bile salts and bile pigments. Van den Bergh reaction on 27-2-45 direct positive biphasic, total bilirubin 9·8 units. A second examination on 22-3-45 showed direct positive delayed, total bilirubin 1·6 units. The main complaint at this time was dyspepsia. Gastric analysis done on two occasions showed the following results:

	Total acidity	*Free HCl* 10-2-45	*Total acidity*	*Free HCl* 8-3-45
Before test mean 38 c.c.	26	14	12	Nil
¼ hr. after ..	1	Nil	1	Nil
½ hr. after ..	5	3	1	Nil
¾ hr. after ..	12	8	2	Nil
1 hr. after ..	42	34	5	3
1¼ hrs. after ..	..	..	28	12

First curve showed hypermotility and suggestive of a reflex condition. The second one done one month later showed diminished total acidity and absence of free HCl in the first four specimens.

Patient was put on calcium gluconate intravenously and hydrochloric acid by mouth but the dyspeptic symptoms still persisted. Van den Bergh reaction on 4-5-45 showed direct positive delayed, total bilirubin 1·2 units. Patient was discharged cured on 30-5-45. This is the only case in which relapse occurred. The previous history of typhoid fever and the arsenical injections might have contributed to the dyspeptic condition that persisted for a long time.

Diagnosis

In a well developed case the diagnosis is always easy, but during an epidemic atypical symptoms sometimes may mislead even an experienced clinician. A young adult coming with a history of low fever, indigestion, constipation, abdominal pain, jaundice of a few days duration, and passing greenish urine and who on physical examination shows a palpable and tender liver with bile pigments in the urine is suffering from infective hepatitis. High fever occurring at the commencement may be mistaken for influenza, dengue or sandfly fever, but within two or three days, appearance of jaundice and the presence of bile in the urine will settle the diagnosis (Case 15). Colicky pains in the abdomen may be mistaken for biliary appendicular, or renal colic. The presence of jaundice will distinguish appendicular and renal colic, but in the case of biliary colic the diagnosis is sometimes difficult. An x-ray photograph for gall stones or a few days observation only can settle the diagnosis. Leptospiral (*L. icterohæmorrhagica*) jaundice can be distinguished by the isolation of leptospira or by the agglutination test. Leucocytosis in the blood is a characteristic feature of leptospiral jaundice, but in some cases it is present in infective hepatitis also. Diagnosis from other forms of obstructive jaundice such as gall stones, parasites, new growths etc. is easy. Primary carcinoma of the liver sometimes causes difficulty, but the hardness of the liver, tenderness and progressive enlargement are in favour of carcinoma. There were two cases in this series that showed this clinical picture and both were more than 45 years old, but routine treatment for infective hepatitis cured the patient and the diagnosis was confirmed. The question of syphilis in relation with infective hepatitis has been dealt with elsewhere in the paper. A series of cases of lobar pneumonia were admitted during the same period and few of them showed toxic and infective jaundice, but this was transient and disappeared in a week. Presence of definite signs of lobar pneumonia made the diagnosis easy. Jaundice in relation with malaria has been discussed elsewhere in the paper.

A young adult male had typhoid fever and B. typhosus was isolated from the urine. He had a relapse and was discharged cured. Six months later during the height of the epidemic of infective hepatitis he was admitted for jaundice, which for all practical purposes looked like the second stage of infective hepatitis. The patient was running a low fever between 99 to 101·0F. Van den Bergh reaction showed only 15 units of bilirubin and it took three months for the jaundice to disappear in spite of all restrictions in diet. In this case hepatitis and/or cholecystitis due to B. typhosus has to be considered.

Treatment

1. Rest in bed: In the first stage it is not necessary, in the second stage it may help the cure, and in the third and fourth stages it is essential. As the condition improves the patient might be allowed to get up and walk about and still later to carry on the daily work of the individual.

2. Restriction of diet: This is the most important of the treatment. During the earlier part of the epidemic, all the patients were put only on barley water, arrowroot congee and fruit juice, but later on dilute milk was added on to the diet from the beginning. As the condition of the patient improved rice and butter milk were added on and still later they were allowed bread, and bland vegetables such as boiled potatoes. Fats were completely withheld. In spite of instructions, some of the patients took a more liberal diet: all the same they got cured with only one difference, the cure was delayed for another week or ten days. Case No. 11 shows that irregularity in diet increases the jaundice but further restriction in diet will cause improvement in the patient's condition resulting in recovery though delayed. In some cases loss of appetite prevents them from eating anything harmful.

3. Saline purgatives: Mag. sulph ½ to 1 oz. in concentrated solution is given every morning during the first week and every alternate day during the second week. Afterwards it is given once a week.

4. Alkalies by mouth: Potassium citrate and potassium acetate in dram (60 grs.) doses three times a day is given as a routine.

5. When colicky pains are severe and when the jaundice is deep intravenous 10 c.c. of 10 per cent solution of calcium gluconate is given. Insulin 5 units a day with glucose is given in addition.

6. When low fever persists for more than a week the patient gets hexamine 10 grs. three times a day.

7. When hæmorrhages are present vitamin K (5 mg.) is given intramuscularly daily or every alternate day depending on the severity of the condition. Calcium and hæmoplastin are given by injection.

8. When cholemia sets in intravenous glucose with soda bicarb is given.

9. Beattie and Marshall (1944) reported very good results with methionine, a sulphur containing compound, in the treatment of infective hepatitis and post-arsenical jaundice. Recently Pollock *et al* (1945) and Higgins *et al* (1945) have tried the effect of methionine, 5 gms. a day and found that it has no effect on the severity or duration of the disease. We had no opportunity of trying this drug.

10. Indigenous method of treatment: (*a*) Local application of castor seeds in honey is used often. One patient admitted into the hospital showed intense congestion of the eyes as a result of local application of this irritant. Three days later the congestion disappeared but deep jaundice could be observed. The local irritant treatment prevents the jaundice being observed but the severity is not affected in any way.

(*b*) Leaves of Euphorbiaceæ family, Phyllanthus Maderaspatensis and Rotundi folis are crushed and taken in butter milk by mouth. Whether this treatment has any beneficial effect on the jaundice or not it is not possible to say at present. Investigation is being carried out and the results will be published in a separate communication.

Discussion

Virchow (1847) from his observations concluded that jaundice can be produced by changes inside or outside the liver and classified it as hepatogenous and anhepatogenous. Minkowski and Neunyn (1886) from their experiments on geese claimed that all jaundice was hepatogenous. McNee (1913) showed from experiments on geese that it was only the stellate cells of Kupffer and not the hepatic cells that were responsible for the formation of bile pigments. These observations were confirmed by Whimple, Mann, Haldeman and others.

Van den Bergh (1918) using diazo reagent (which is now called Van den Bergh reaction) showed that there were two types of bilirubin one direct and the other indirect, and classified jaundice as mechanical and dynamic.

McNee (1923) classified jaundice under three headings:—

1. Obstructive hepatic jaundice. Jaundice is deep, bile is present in the urine, but occasionally absent from the motions, and Van den Bergh reaction is direct positive immediate, indirect positive.
2. Toxic and infective hepatic jaundice. Jaundice is either light or deep, urine contains bile, motions contain bile and Van den Bergh reaction is direct positive biphasic, indirect positive.
3. Haemolytic jaundice. Jaundice is mild, bile is absent in the urine, motions contain bile, and Van den Bergh reaction is direct positive delayed, or indirect positive.

Rich (1930) has classified jaundice under two headings:—

1. Retention jaundice, which corresponds to hæmolytic jaundice.
2. Regurgitation jaundice, which corresponds to obstructive jaundice.

According to the present accepted view bile pigments are formed from the blood by the cells of the reticulo-endothelial system which are present all over the body, liver, spleen, bone marrow etc., and these pass through the polygonal cells of the liver into the bile capillaries.

Four different reactions occur when Van den Bergh reagent is added to the blood plasma (Beaumont and Dodds, 1944).

1. Direct immediate reaction. Bluish violet color appears immediately and reaches the maximum in ten to thirty seconds.
2. Direct biphasic reaction. Red colour appears immediately and changes into violet after some time.
3. Direct delayed reaction. The colour develops in fifteen minutes.
4. Indirect reaction. The colour appears only after the addition of 96 per cent alcohol and saturated ammonium sulphate.

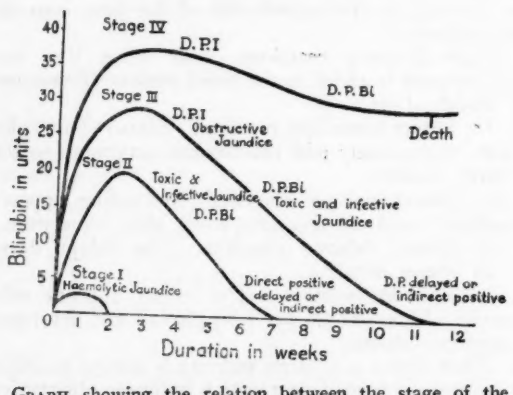
When direct is positive indirect is always positive. Direct positive immediate reaction indicates obstructive jaundice, direct positive biphasic, toxic and infective jaundice; direct delayed and/or indirect reaction indicate hæmolytic jaundice. Blood has to be examined within two hours; otherwise the interpretation becomes difficult. Blood plasma that shows direct positive immediate reaction in two hours will show direct positive biphasic if tested after four hours.

In the present paper McNee's classification has been adopted. All the three types of jaundice were observed in infective hepatitis. As stated earlier in the paper the first stage or the stage of 'hæmolytic' jaundice indicates a mild infection and either gets cured or goes on into the second stage or the stage of toxic and infective hepatic jaundice. The patient might get cured in the second stage or go on to the third stage or the stage of obstructive hepatic jaundice. In this stage also the patient recovers unless complications set in. The fourth stage represents the final stage of infective hepatitis, resulting in cholemia and death. Probably Gregory (1933) is the only author who has pointed out hæmolytic jaundice as a clinical entity in infective hepatitis. Clinical diagnosis is easy during an epidemic

of infective hepatitis, and the direct delayed or indirect positive Van den Bergh reaction confirms the diagnosis. All the fifteen cases of hæmolytic jaundice observed during this epidemic were diagnosed clinically.

The transition from the hæmolytic to the toxic and infective hepatic jaundice could not be shown by the biochemical reactions. Mild infections get cured in the first stage itself and in other cases the development of the jaundice was so rapid that it was not possible to have the blood examined at the stage of transition. But when the patient in the toxic and infective stage of jaundice gets cured the jaundice reverts back to hæmolytic or first stage. Patients admitted during the second stage and passed on to the third stage showed clearly the transition of the toxic and infective hepatic jaundice to the obstructive hepatic jaundice. During the process of recovery of patients in the third stage, the reversion from the obstructive hepatic to the toxic and infective hepatic and finally to the hæmolytic jaundice could be observed.

The accompanying graph will show the relationship between the stage, the duration of the jaundice and the amount of bilirubin in the blood.



GRAPH showing the relation between the stage of the disease and the amount of bilirubin in the plasma.

1. Hæmolytic jaundice—Is cured or develops into second stage.

2. Toxic and infective jaundice—Is cured or develops into third stage.

3. Obstructive hepatic jaundice—Is cured or goes on to the fourth or the final stage.

Death might occur in the second stage when complications such as dysentery or pneumonia occur as in one of the cases (No. 22).

The jaundice in the first stage is due to the damage of the liver cells resulting in the accumulation of indirect bilirubin in the blood stream. In the second stage some of the damaged liver cells cause obstruction and both types of bilirubin direct and indirect are present. In the third stage obstruction to the bile capillaries is the dominant feature, but in some cases the obstruction is not complete and bile is present in the motions.

If the jaundice is mild and urine contains bile pigment the patient is at the commencing stage, and if the jaundice is severe and urine contains only traces of bile the patient is in the stage of recovery. This has been observed very often during the present epidemic of infective hepatitis.

The so-called pre-icteric stage or the stage of latent jaundice has been included in the first stage or the stage of hæmolytic jaundice. Mild jaundice has always been observed during this epidemic and Van den Bergh reaction has confirmed the diagnosis by the direct positive delayed or indirect reaction.

Dissociated jaundice was observed in four of the ten cases investigated. Bile pigments were present but bile salts were absent, and was observed only during the last few days before discharge from the hospital as cured. The bilirubin content in these cases varied from 5 to 8 units at the time the dissociation occurred. French school is very clear on the condition of dissociated jaundice and according to Boyd (*loc. cit.*) further work is necessary before it can be accepted.

Quantitative estimations of the total bilirubin during the development of the recovery stage have shown that the rate of increase at the commencement is very marked while during the recovery stage the rate of fall is small, 1·2 to 2·5 units per day and during the final phases of recovery 0·05 to 0·5 units per day. On an average the fall of bilirubin can be said to be 1·0 to 1·5 units per day.

SYPHILIS IN RELATION WITH INFECTIVE HEPATITIS

Although jaundice has been observed in the beginning of the sixteenth century (Paracelsus, 1510) during the secondary stage of syphilis the recognition of this condition as a clinical entity was made only in the middle of the nineteenth century by Portal, Ricord, Gubler, Lancereaux, Werner and others. The jaundice in these cases is due to the toxic degeneration of the liver cells and not due to the actual invasion of the liver cells by the spirochetes (Sagar 1936).

The introduction of arsenical preparations in the treatment of syphilis has considerably increased the incidence of jaundice. Worster-Drought (1940) has classified jaundice after arsenical treatment under three headings. (1) An early type occurring within a few hours or a few days after the injection. (2) A delayed type occurring within a few days or a few weeks and more severe than the previous one. (3) A severe type causing extreme degeneration of the liver cells and resulting in death.

Sagar (1926) after a review of the literature has come to the conclusion that post-arsenical jaundice is entirely different from epidemic infective hepatitis but the two diseases may exist together.

Seven cases of the present series gave a history of syphilis and blood Wassermann was positive in all the cases. Only one case gave the history of injections of arsenic three months ago. He was a young adult of 25 years who came with a history of jaundice of 20 days' duration. Jaundice was deep, liver was enlarged, urine showed bile salts and pigments, and

blood Van den Bergh showed direct positive immediate, indirect positive, total bilirubin 66·0 units. He was given the routine treatment and at the end of 10 days Van den Bergh reaction showed direct positive biphasic, indirect positive, total bilirubin 20·0 units. The patient was discharged cured from the hospital after a stay of 57 days.

Dr. Nair, Venereal Specialist of King George Hospital has observed the great increase of jaundice in patients undergoing antisyphilitic treatment with arsenic during and after the epidemic of infective hepatitis. The condition could not be distinguished from infective hepatitis, clinically. Two patients who came for the treatment of syphilis showed jaundice and in both the cases blood Wassermann was strong positive and never had any arsenic. They passed through the typical course of infective hepatitis and was cured with the routine treatment for infective hepatitis after an interval of four and six weeks respectively.

The epidemiology of the disease shows the fundamental difference *i.e.* post arsenical jaundice is not infective whereas infective hepatitis can be transmitted from one individual to another. Barring the infectivity, symptoms, physical signs, course and treatment are the same in both. Both the conditions might exist together, and it usually happens when the patient is given arsenic during the incubation period of infective hepatitis. The jaundice in such cases will be deeper and toxæmia more, but with the main difference that, hæmorrhages do not occur in post-arsenical jaundice.

Recently post-arsenical jaundice has been claimed to be produced by improper sterilization of syringes, Solmon *et al*, 1944; Shechan 1944).

Cholesterol Metabolism

Epstein (1932) investigated the cholesterol content of four cases of infective hepatitis (catarrhal jaundice) and found that it varied inversely with the intensity of the jaundice. The diminution was mainly in cholesterol esters and as the jaundice improved both the total cholesterol and esters came up to the original level and in some cases rose above normal. In cases of obstructive jaundice as a result of stones, strictures, new growths, etc., the cholesterol content was increased and was directly proportional to the intensity of the jaundice. Normal level was restored after the disappearance of jaundice. Rolleston and McNee (1929) observed the increase in cholesterol content of the plasma in cases of obstructive jaundice. Only one case (stage III) in the present series showed a low cholesterol content (65 mg.) and later an increase to 112 mg. per 100 c.c. Two other cases (stage II) showed an initial cholesterol of 177·4 and 177·8 mg. and which later fell to 127 and 137·5 mg. per 100 c.c. Definite conclusions could not be drawn from these small number of cases.

Animal Experiments

Anderson (1937) succeeded in the transmission of infective hepatitis from man to pigs. Cameron (1943) injected whole blood, plasma or leucocytic fraction from cases of infective hepatitis in different stages into monkeys, guinea pigs, dogs, mice, rats and hamsters but failed to transmit the disease to these experiment animals. All the animals showed leucopenia. Post-mortem of one case showed necrosis of the liver cells and another round cell infiltration of the portal canal.

Blood of five and urine of two patients were inoculated into guinea pigs. These experiments were done in collaboration with Dr. N. G. Pandalai, Professor of Bacteriology, Andhra Medical College and the results are given below:—

I. Blood Inoculation

Guinea Pig. A. Three to four months old. Weight 184 gm.

21-9-44. Five c.c. of blood from a patient during the second stage was inoculated intraperitoneally. The animal did not show any symptoms. Van den Bergh reaction of blood on 9-10-44 showed negative results. The animal died on the night of 24-10-44, weight 181 gm. Post mortem done the next day showed only slight fatty changes in the liver without any evidence of necrosis of the liver. No well-defined changes were observed either in the spleen or the adrenals. Kidneys showed slight cloudy swelling of the tubular epithelium and lungs congestion and interstitial inflammation.

Guinea Pig. B. Three to four months old. Weight 190 gm.

21-9-44. Five c.c. of blood from a patient during the third stage was inoculated intraperitoneally. The animal showed no symptoms. Van den Bergh reaction on 5-10-44 showed both direct and indirect negative. The animal is still alive.

Guinea Pig. C. Three to four months old. Weight 225 gm.

21-9-44. Five c.c. of blood from a patient during the third stage was inoculated intraperitoneally. The animal showed no symptoms. Blood Van den Bergh reaction on 9-10-44 showed direct negative and indirect negative. The animal was killed on 9-10-44. Post-mortem weight 229 gm. Adhesions were present between the liver and the anterior surface of the stomach, and between the spleen and the surrounding structures. Liver showed no well-defined areas of necrosis, but the nucleus of some of the liver cells appeared more condensed and some more eosinophilic. Spleen showed slight lymphoid hyperplasia. Other organs were normal.

Guinea Pig. D. Three to four months old. Weight 300 gm.

Five c.c. of blood from a patient during the third stage was injected intraperitoneally on 25-9-44. The animal did not show any symptoms and Van den Bergh reaction on 17-10-44 showed direct negative, indirect negative. The animal died on 18-10-44. Post-mortem: Weight 355 gms. Medulla of the adrenal was normal but the cortex showed cells loaded with lipoid. All the other organs were normal.

Guinea Pig. E. Three to four months old. Weight 295 gm.

25-9-44. Five c.c. of blood from a patient during the third stage was inoculated intraperitoneally. The animal did not show any symptoms and Van den Bergh reaction on 18-10-44 showed direct negative, indirect negative. The animal is still alive.

II. Inoculation of Urinary Sediment

Guinea Pig. F. Three to four months old. Weight 318 gm.

22-10-44. Fifteen c.c. of urine from a patient during the third stage was centrifugalised (3000 revolutions per minute) for 15 minutes, the sediment was suspended in 1 c.c. of normal saline and injected intraperitoneally. The animal did not show any symptoms and is still alive.

Guinea Pig. G. Three to four months old. Weight 525 gm.

The urine of a patient during the third stage was centrifugalised as in the previous case and injected intraperitoneally on 25-10-44. The animal did not show any symptoms and Van den Bergh reaction showed both direct and indirect negative. The animal is still alive.

Although the disease was not transmitted to the experimental animals by inoculation with blood and urine of patients with infective hepatitis two animals showed microscopic changes in the liver, one fatty degeneration and the other condensation of the nuclei and prominent eosinophilic staining. Leucocytic count showed varying results. Van den Bergh reaction of the blood showed both direct and indirect negative.

Summary

1. A study of 312 cases of infective hepatitis occurring during a period of ten years (1935-1944) was made. An epidemic in a mild form occurred in 1942 and appeared in a severe form in 1944 as shown by 197 admissions during that year.

2. The literature of infective hepatitis has been reviewed.

3. The aetiology is discussed.

4. The disease is mainly one of young adults usually occurring between the ages of 16 and 35, the minimum age was 4 and the maximum 60.

5. The minimum incubation period observed was 3 days and the maximum 30 days.

6. Infective hepatitis has been classified under four stages. The first or the stage of hæmolytic jaundice, the second or the stage of toxic and infective hepatic jaundice, the third or the stage of obstructive hepatic jaundice, and the fourth or the terminal stage. The symptomatology of the disease is described in detail under the different headings.

7. Gastric analysis did not reveal any change except the presence of bile in larger number of specimens. Blood cholesterol showed contradictory figures. Fragility was normal in all the cases except in one that showed slight increase. Hippuric acid test done in one case showed normal liver function, but lævulose tolerance test in another case showed some damage to the liver. Urinary diastase was normal in all the cases investigated.

8. Differential diagnosis between the different forms of colic, leptospiral jaundice, and other forms of obstructive jaundice was given.

9. Treatment consists in restriction of diet, saline purgatives and alkalies by mouth, injections of insulin, calcium gluconate when the jaundice is severe, hexamine in cases of persistent fever and intramuscular injections of vitamin K in cases of hæmorrhage. Indigenous methods of treatment are described.

10. The onset, progress and course of jaundice in the different stages of infective hepatitis are discussed. The role of arsenical therapy in syphilis, and cholesterol metabolism are also discussed.

11. Three deaths (1 per cent) occurred and post-mortem was available only in one case.

12. Blood of five and urine of two patients were inoculated into experimental animals and the results were negative.

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References

Barber, H.—*Brit. M. J.*, **1**:87, 1937.

Beaumont, G. E. and Dodds, E. C.—Recent Advance in Medicine. J. & A. Churchill Ltd., 1944, p. 150.

Beattie, J. and Marshall, J.—*Nutrition Abstr. & Rev.*, **14**:326, 1944.

Boyd, W.—Pathology of Internal Diseases, Henry Kimpton, London, 1940, p. 150.

Cameron, J. D. S.—*Quart. J. Med.*, **11**:139. 1943.

Damodaran, K. and Hartfall, S. J.—*Brit. M. J.*, **1**:587, 1944.

Frazer, E. M. R.—*Ibid.*, **1**:701, 1935.

Gordon, I.—*Ibid.*, **1**:807, 1943.

Gregory, H. H. C.—Diseases of Infancy and Childhood. Oxford Medical Publications, 19.3, p. 548.

Higgins *et. al*—*Brit. M. J.*, **1**:401, 1945.

Lucke, B.—*Am. J. Path.*, **20**:471, 1944.

Idem—*Ibid.*, **20**:595, 1944.

McNee, J. W.—*Proc. Roy. Soc. Med.*, **126**:577, 1932.

Neuman, J. L.—*Brit. M. J.*, **1**:61, 1942.

Ottenburg, R. and Spigel, R.—*Medicine*, **22**:27, 1943.

Rolleston, H. and McNee, J. W.—Diseases of the Liver, Gall-bladder and Bile Ducts, Macmillan & Co., Ltd., London, 1929, p. 552.

Sagar, R. V.—*Arch. Int. Med.*, **57**:666, 1936.

Salman, M. R. *et al*—*Lancet*, **2**:7, 1944.

Sheeham, H. L.—*Ibid.*, **2**:8, 1944.

Soffer, L. J.—*Arch. Int. Med.*, **53**:809, 1934.

Wilson, C., Pollock, M. R. and Harris, H. D.—*Brit. M. J.*, **1**:399, 1945.

Worster-Drought, C.—Neurosyphilis. John Bale & Sons. Staples Ltd. London, 1940.

Note—Several papers have been consulted and only some of them are given. It was not possible to get the originals of some of the papers and only abstracts or quotations given by others were available for reference.

PSYCHOSURGERY

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Polonius: Mad let us grant him, then:
and now remains
That we find out the cause of this effect;
Hamlet. Act II, Sc. ii.

This paper is presented as an introduction to a new sub-division of neurosurgery, *viz.*, psychosurgery, before the medical profession. No detailed experience of our series has been given, as they are the subject matter of another paper, but the growth and development of psychosurgery have been traced with possibilities of the future. If this article rouses interest in the minds of the growing generation of enthusiastic Indian surgeons to investigate and research in this field, the publication of this paper will have more than served its purpose.

The surgery of the brain is as old as man himself. Strangely enough operations on the head either on the living or on the dead seems to have attracted the attention of Man through the ages. Records of excavation at Ur of the Chaldees, and at Babylon suggest that some sort of opening of the skull used to be practised by the Sumerians (circa 4000 B.C.) whether as a sort of mutilation, or as a religious ceremony or as a measure of treatment for illness it is difficult to say. Mummies unearthed in Egypt have shown that the operation of opening the skull, or as it was called trephining was not unknown to the inhabitants. Primitive surgery, much of it enforced by the necessities of personal and tribal strife, included all the rudiments of the art. By means of sharpened flints or teeth of fish, trephining of the skull was undertaken. Among the hoary superstitions by which men have always been beguiled, that which is concerned with belief in the "possession" of the human body and mind by demons is perhaps the most interesting. For the relief of this malady of "possession" the aid of the surgeon was not infrequently invoked in prehistoric times. This, the most remarkable of all primitive surgical procedures, was performed to cure headache and to allow the escape of evil spirits of epilepsy or lunacy, and there are many prehistoric skulls that testify to the successful performance of this formidable operation. Trephining is as old as surgery itself.

The evidence of prehistoric trephining stands conclusive, even if the reasons for the institution of this measure must remain in the realm of conjecture. Some respect, certainly a mixed respect must be felt for those who, without a precise knowledge of brain function, and in the absence of anæsthesia and asepsis, undertook the hazardous assault on the cranium. Recovery was not an uncommon result, paleopathologists have shown us. The trepanations of a later, though scarcely advanced period held out no better prospect of recovery. Hudson's figures for the close of the last century for Guy's Hospital of London, England, showed an overall mortality of 75 per cent, for intracranial surgery, while conservative estimates of the results of the success of the healers of Gazelle Peninsula and Duke of York Islands of Blanche Bay, put it as high as 70 per cent. Though much of the surgery of the skull and brain was performed as the result of injuries inflicted during tribal warfare, there are indications that these operations were performed for the relief of pain, and to allow evil spirits to escape. Whether those evil spirits escaped through the opening in the skull or fresh ones entered, it is difficult to say, but it is agreed from evidences on the skull that the patients survived the operation for a considerable time.

It is a surprising fact, as has been proved, that so severe an operation as trephining the skull was attempted as far back as the early stone age—a phenomenon which can be better understood in the light of the love of operating and surgical dexterity found in many of the present day aborigines. Trephined skulls from the neolithic period have been found in most of the European countries, in Algiers, the Canaries, N. America, Mexico, Peru, Argentine, etc. Well cicatrised trephine holes in many of these skulls prove that this severe operation had been performed two or more times on the same individual. The indications for trephining, if a deduction from the conditions existing amongst present day aborigines is permissible, may have been headaches, convulsions and mental disorders.

The operation of trephining was not unknown in India. It was definitely practised nearly 2000 years ago, though an orderly technique as evolved by the islanders of New Britain and New Ireland are lacking. Various indications for this operation have been mentioned in different parts of the world, but it is curious whether one race believed in evil spirits, and the other in deranged humours of any particular pathology they fancied, practically all these people have utilised this operation in various mental disorders including epilepsy and convulsions.

Just as primitive surgery of the brain was an outcome of the necessities of tribal warfare, the present position of intracranial surgery was largely the result of the brain injuries of World War 1914-1918. 'Out of evil cometh good'. It was due to the pioneering work of Harvey Cushing, Horseley, Foerster, Dandy, Adson and others that the surgery of the brain was laid on firm foundations. Advances in anæsthesia, more precise knowledge of the functions of the brain, the development of the electro-surgical unit for controlling that formidable terror of neuro-surgeons, *viz.*, hæmorrhage, have in no small measure contributed to the rapid advancement of neurosurgery. Most of these surgical procedures were for injuries of the brain and its sequelæ, for abscesses and tumours.

The surgery of mental diseases was in reality one of the oldest branches of surgery, if not the forerunner of other surgical procedures. The conception and reason for such a procedure may have been incorrect from later knowledge of the physiology, pathology and functions of the brain; but it is, however, an indisputable fact that often the aid of surgery was sought in the alleviation, if not cure of mental diseases.

The conception and attitude of the public to the unfortunate mentally deranged has been most varied in different countries at different periods of time. The mentally afflicted was looked upon with horror and was confined in jails with heavy chains and no torture or punishment that human mind could devise was considered sufficient to exercise the devil. No wonder that the mental state of such an unfortunate rapidly grew worse only to be mercifully relieved by death. Such was the state of affairs in Europe including the United Kingdom till the turn of the last century. In the countries of the middle east, where the Moslem faith predominates, the mentally afflicted was more fortunate, as he was a person for veneration, as it was surmised that the acts of such a person were not his own, but was prompted by the Almighty. Whatever might have been the attitude and treatment of such people, mental disease was elevated to a science and art in Great Britain by the brilliant and untiring effort of Henry Maudsley. From the beginning of the present century the science of psychiatry has been steadily progressing, thanks to the great work of neurophysiologists like Sherrington, Ramony Cajal, Forester and Broadmann, and of psychologists like Sigmund Frued, Jung and Adler. With greater knowledge of cerebral pathology and cerebral localisation and an increased interest in the biochemistry of the brain, all made possible by the rapid advance of neurosurgery, psychiatry made rapid strides. It was only a question of time that modern knowledge and methods of surgery would invade the field of mental diseases in a rational manner.

This brings us to a new branch of neurosurgery, *viz.*, psychosurgery. Psychosurgery consists in surgical operation on the anatomically intact brain for the purpose of relieving mental symptoms. It was first devised and named by Egaz Moniz, the distinguished Portugese neurologist, essayist and diplomat, following the Third International Neurological Congress in 1935, at which time a remarkable symposium was offered on the function of the frontal lobes. Approximately a year later Moniz published his monograph detailing his results in his first twenty cases.

With the advance of mechinisation and the infliction of varieties of injuries to the brain by missiles, it was observed that life was compatible in the absence of large masses of brain tissue. The well publicised 'American Crow bar case' where a large crow bar seems to have been driven across, mutilating both the frontal lobes, and the patient's subsequent recovery first suggested that the frontal lobes could be removed without danger to life. Later, deliberate, successful unilateral and bilateral frontal lobectomies have been performed without detriment to the life of the person. Observations of persons, with frontal lobectomy, and experimental extirpations of frontal lobes in monkeys and chimpanzees were then resorted to.

Moniz (1936) had observed that in individuals with organic lesion of the frontal regions were followed by varying degrees of loss of tension, and the production of a more happy easygoing personality. He, therefore entertained the hypothesis that doubt, indecision, worry and anxiety were mediated through arcs in the frontal regions, and argued that if these pathways could be destroyed, the individual could then exist on a much more comfortable level. Bianchi after experimental damage to the prefrontal areas of the brain of monkeys, came to the conclusion that the damage tends to "disagregate the personality and incapacitate for serialising and synthesising groups of representations." Jacobsen experimentally established the fact that "destruction of the frontal areas is followed by failure to adjust to delayed-response tests."

Hebb and Penfield (1940) have investigated human behaviour after extensive bilateral removal of the frontal lobes. A case of traumatic injury had destroyed somewhat less than 1/3 of each frontal lobe and left a scarred zone in each hemisphere, giving rise to continuing abnormal electrical potentials and to recurring epileptic seizures. Surgical removal of scars and a zone of grossly normal cerebral tissue, in such a way as to insure a minimum of scar, resulted in comparative freedom from attacks. Although after operation a 1/3, and possibly more, of the total volume of each frontal lobe was lacking, there was a striking postoperative improvement in personality and intellectual capacity, with the same medication as before the operation. After the initial postoperative period no clinical or psychometric evidence of deterioration was detected. They concluded that "abnormal areas of brain may produce in a positive sense both decreased mental capacity and abnormalities of behaviour, and the absence of these areas may allow other parts of the brain to recover their normal function. It is concluded that removal of a third of both frontal lobes uncomplicated by pathological change in the rest of the brain need have no grossly deteriorating effect.

With these experimental data in the background Moniz (*loc. cit.*) devised the operation of prefrontal leucotomy in mental diseases. To quote Moniz: "the idea was to operate upon the brains of patients, not directly upon the cell groups of the cortex or of other regions, but rather by interrupting the connecting fibres between the cells of prefrontal area and other regions, *i.e.*, to say by sectioning the subcortical white matter. As a result of the interruptions of the cylinder axes the cells of the prefrontal area and of other regions of the brain connected with these would be affected secondarily."

". . . . it can be affirmed now that these operations are not prejudicial to either physical or psychic life of the patient, and also that recovery or improvement may be obtained frequently in this way."

Moniz (*loc. cit.*), in discussing the theory which led him to propose prefrontal leucotomy, considers that whereas in normal people the functional connections between the cortical cells are variable, giving rise to innumerable different groupings in certain mental disorders, some functional groupings become more or less fixed and give rise to obsessions and delusions. Mental improvement may become possible by cutting the association fibres concerned in these persistent pathways. He was cautious, and in his first twenty cases tried on chronic patients, whose prognosis was poor. The results encouraged further trial. Some improved, and there were no deaths, and none of them were worse after the operation.

Consideration of the physiology of the frontal lobes shows that the operation is based on sound principles. Injury to the frontal lobes results chiefly in alterations in behaviour, as is well exemplified in the American Crow bar case. Behaviour changes have also been noted after the surgical removal of the frontal lobes in man and animals. Distractibility, lack of restraint and boastfulness have been reported by Brickner (1939), and slowness, deliberate activity, perseverance and freedom from anxiety by Ackerly (1935). Similar changes have been noticed in experimental animals. This work has shown that removal of frontal areas gives rise to some form of deficiency that has been termed 'intellectual'.

The operative technique of prefrontal leucotomy has undergone many modifications, and no two clinics seem to follow the same identical procedure, but the purpose and the principle, *viz.*, severing the white matter of the prefrontal cortex as efficiently as possible with the least damage to the grey cortex and blood vessels remains the same. Moniz in his early cases exposed the frontal cortex by a superior approach close to the middle line, and alcohol was injected to the subcortical white matter, and later crushed by a leucotome with a steel loop. He modified this leucotome by using a steel band to cut rather than crush the subcortical white matter.

His technique of approach consisted in making trephine openings about 1 to 1·5 cms. in front of a vertical line passing through the base of the tragus and 3 cms. to either side of the midsagittal line. The leucotome is introduced to a depth of 4·5 cms. in an anterolateral direction, the loop is opened, and the instrument turned so as to cut a core 1 cm. in diameter in the white matter; the blade is then retracted into the instrument which is withdrawn 1 cm. and a second core is cut at 3·5 cms., and finally a third at 2·5 cms. from the surface of the brain. No tissue is removed. The leucotome is then withdrawn entirely and reintroduced in an anteromesial direction to a depth of 4 cms., where the first section is made, withdrawn 1 cm. in order to cut a second core at 3 cm., and a final section is made at a distance of 2 cms. from the surface of the brain. Moniz has further extended the above technique cutting six cores on each side. He is of opinion that by this more extensive attack, not only are the complications fewer and transitory, but the clinical results are better.

In the various types of operations, two broad varieties can be recognised. Firstly, those who follow the open method where a large osteoplastic flap of skull is raised on both sides, the brain exposed, and the white matter sectioned under direct vision. In the second variety, the brain is approached through small trephine openings and the white matter sectioned blindly.

The open method consists in turning a suitable osteoplastic flap, the dural vessels ligated and the brain exposed by a crucial incision in the duramater. An avascular gyrus is chosen and an illuminating speculum introduced, and the white matter cut under direct vision in different directions at different depths. The site of the osteoplastic flaps varies with different neurosurgeons. In a small series of six cases performed at the Mayo Clinic, U.S.A., a superior approach was used by Moersch. Lyerly (1938) in a more extensive trial prefers a lateral osteoplastic flap. Whichever route is employed, the sectioning of the white matter is always under direct vision after the introduction of an illuminated speculum into the brain. This open method is fundamentally sound, and must appeal to all neurosurgeons who hate a blind procedure, but it has the great disadvantage of being a very formidable surgical undertaking with its associated grave dangers. The advantages and disadvantages of the open method in contrast with the closed method will be discussed later.

The closed method essentially consists in making small holes in the skull either with a small trephine or burr and the white matter sectioned blindly by introducing a suitable instrument through these openings. The various methods of operating by the closed method differ in (*a*) the site of the trephine or burr opening and (*b*) the type of instrument or 'leucotome' used in sectioning the white matter.

The site of burr hole in the original Moniz technique was situated in the superior part of the skull about 3 cms. on either side of the midsagittal line, the leucotome being inserted in a downward and lateral direction. The advantage of this superior approach was that there was less risk of injuring the main branches of the anterior cerebral artery on the mesial surface of the brain, but a correspondingly greater one of injuring the grey matter of the orbital surface of the frontal lobes. In addition, it was difficult to estimate the amount of white matter, and consequently it was by mere conjecture that the depth to which the leucotome could be effectively and safely introduced was determined. To offset these disadvantages Freeman and Watts (1939) approached the prefrontal area by a lateral approach. The lateral approach involves no risk to the orbital grey matter of the prefrontal lobe. The branches of the anterior cerebral artery, theoretically exposed to a greater risk of damage, it is not in reality so, as a more accurate estimate of the thickness of the white matter can be made, and consequently the leucotome can be introduced to the requisite depth without fear of injuring blood vessels on the mesial surface of the brain.

A series of measurements in the cadavers were made to determine the relative thickness of the white to the grey matter at the proposed level of section. The bodies were those of gold miners who had died of accidents, and the post-mortem conducted about six hours later. No reason was felt to presume that the proportion of white to grey matter was any different between the living and the dead; at least not to any extent to affect the technique of the operation. It was found that on each side the total thickness of the grey matter on either side of the central core of white matter was equal to the thickness of the white matter. Therefore it was easy to estimate the thickness of the white matter in each prefrontal lobe by measuring the diameter of the brain with callipers at the site of burr holes. The thickness of the white matter on each side

is ¼ the diameter of the brain and so the leucotome could be introduced up to ⅜ of the diameter of the brain, to include the peripheral thickness of grey cortex.

In the cases treated at the Government Mental Hospital, Bangalore, S. India, the lateral approach as described by Freeman and Watts was followed with slight modifications, the details of technique followed having been described in another paper by us (Balkrishna Rao and Govindaswamy, 1944).

Various instruments have been used to section the white matter. Moniz in his early cases used a needle both to cut the white matter, as well as to inject alcohol. Lyerley made use of a blunt brain knife to cut the white matter under vision. Later Moniz devised a metal wire, which when pushed out of the instrument would form a loop like a polypus snare. The rotation of the instrument would cut a core, and the wire could be withdrawn into the body of the instrument before the latter was removed from the brain. Freeman and Watts (*loc. cit.*) simplified the procedure by using a Killian's nasal elevator. McGregor and Crumbie (1945) devised a leucotome with a knee screw action to cut a section of 2·5 cms. at any desired depth.

Both Killian's nasal elevator and the McGregor and Crumbie leucotome have been used by us with equal success. Due to an unfortunate accident with the latter instrument, a simplified, but yet safe and incorporating all the advantages of the McGregor and Crumbie leucotome was sought. This simplified leucotome devised by us (Balkrishna Rao and Chandrasekharan) is essentially a Killian's leucotome, graduated in centimeters. The blade is hollow to the tip, and at the proximal end a Record syringe can be attached. The instrument is simple to handle and is devoid of risk.

The closed method of operating though not so appealing as the open operation, has the great advantage that the procedure is simple and fairly rapid. The advantage of the open method is that there is practically no risk of hæmorrhage by the inadvertent injury of an artery and consequent non-recognition or impossibility of stopping it. In the closed method, in practice, however, such a complication seems remote, and recorded deaths in the literature due to injury of blood vessels have been few. The operation by the open method has an inherent mortality on account of the extent and range of the operation, which factor is if not non-existent, is at least negligible by the closed method. There is nothing to choose in the end results of either the open or the closed method of operation; naturally the closed method of operation is the favoured type by most surgeons.

Different anæsthetic agents have been used in the performance of this operation depending on the experience of the surgeon and the availability of suitable drugs and administrators. Local anæsthesia, gas and oxygen, rectal avertin, intravenous anæsthesia, cyclopropane, chloroform etc., have all been used. In our experience open administration of chloroform is as good as any, being quite safe, efficient and one with which most of the staff are familiar.

Before the introduction of surgical procedures the treatment of many mental disorders was by inducing convulsions, and thereby producing a shock to the general nervous system. It was surmised that this intensive shock produced some biochemical changes in the brain with subsequent improvement of the mental disorder. Sakel (1934) induced convulsions by injecting very large doses of insulin, producing a rapid hypoglycæmic state, thereby producing convulsions and shock. On account of the great dangers of the hypoglycæmic state and the variable response of different individuals to the same dose of insulin, Meduna (1937) introduced intravenous administration of cardiazol as the convulsant. This drug though safer than insulin, was certainly difficult to cut short the convulsive seizure at any desired moment. This led Cerletti and Bini to introduce the electrical method of inducing convulsions, which has the advantage that the convulsions can be carefully controlled, and can be cut short when desired. This method is certainly a great improvement on the chemical convulsants. When convulsion therapy was introduced, a great deal of enthusiasm was evinced and a large amount of success was claimed for this mode of treatment. When the first wave of enthusiasm had subsided, and after an extensive trial at various centres were evaluated, it was a surprise to find that the expectations of the early days of convulsion therapy had not been realised. In the few cases that did respond to convulsion therapy, many regressed to their original state after a time. One of the disappointments, apart from such complications as fractures and dislocations that occurred during the convulsive state, has been the frequency with which some patients relapse when treatment is discontinued. This necessitates a sort of maintenance treatment. Horace Hill (1942) writing in the *Lancet* says, "In a New York state hospital a thousand schizophrenics treated with convulsive therapy did even worse than an equivalent control group left untreated."

While not attempting to detract from the undoubted merit of convulsion therapy in a few selected cases, it appears justifiable to assume that a large number of cases would get greater and lasting relief by leucotomy. It is not the intention to advocate the abandoning of convulsion therapy, but to suggest that there is no justification to deny early surgery when a reasonable trial with convulsion therapy has failed to give permanent relief. Except in a few cases it is difficult and often impossible to keep a maintenance treatment with convulsion therapy even in those in whom such therapy has been of benefit.

One of the most encouraging features of this operation is the almost immediate improvement associated with a very low operative mortality. Rizatti and Borgarello had no deaths in a consecutive series of 185 cases, Dax and Smith (1943) had two deaths in 50 cases, we had one death in 39 cases, Freeman and Watts (*loc. cit.*) twenty in 204 cases. Considering the type of patient and the operation, the mortality rate is certainly not discouraging. The improvement in the mental condition of the patient is still more encouraging.

Two aspects of the question of improvement have to be considered before figures could be calculated regarding the percentage. A patient who after operation is able to take care of himself, attend to ordinary duties and shoulder the responsibilities of his station of life, and very often a useful earning member of society is definitely 'cured' in the ordinary sense of the term. A second type of case where the patient is violent, maniacal and a source of danger due to homicidal and suicidal outbursts of temper, with loss of orientation and filthy habits is a problem both of management and of finance to relations as well as to mental institutions. Such a patient needs constant and careful supervision, and the worry, anxiety and the financial strain to a large family with poor economic status needs no comment. The need to keep such patients indefinitely in institutions is certainly a great responsibility and a drag on the resources of the state. If such a patient after leucotomy, were to be able to look after his ordinary needs of daily life, and is not a source of danger either to himself or to his neighbours, and is able to understand and carry out simple actions, he would be certainly a great improvement on his pre-operative condition. Though intellectual improvement of any great order has not occurred, such a patient is easily looked after and managed. These may be considered 'improved'. Taking these criteria as good results, Freeman and Watts (*loc. cit.*) in a survey of 170 cases over a period of six years have obtained 61 per cent of good results. The results in our short series of 39 cases have been encouraging; nearly 2/3 of our cases have been good. In some cases where no improvement has occurred after the first operation, re-operation at slightly more posterior levels has been followed by good results, though in our series no case of failure has yet been submitted to a second operation.

The experience gained at the Mental Hospital at Bangalore has been one of great encouragement. The majority of cases chosen for operation, were those where convulsion therapy had completely failed after repeated trials. They were considered as hopeless, and the ultimate prognosis was necessarily very gloomy. With such a material, it is a matter of profound gratification that quite a fair proportion of them improved after leucotomy, and a number of them are leading happy and useful lives as housewives, engineers, school masters, and farmers.

In view that the pathological processes and causes of these mental disorders are not well understood, criticism of this operation is neither wanting nor unexpected. Nichols and Hunt (1940) are of opinion: "We must realise that we are substituting one disease for another, and although this may be a perfectly justifiable procedure in severe cases, it can never be used in those individuals whom we wish to return to a reasonably high economic and social level." True, the pathology of mental diseases is not well understood, the functions of the frontal lobe still under a cloud of surmise, but looking back to the development of medical science, one often sees brilliant examples of successful treatment preceding correct conceptions of cause and effect. Syphilis existent in all countries used to be treated successfully long before its etiology and pathology were well understood. Amoebic dysentery was treated efficiently with ipecacuanha before either amœba or emetine was known. The certain cause of cancer still awaits elucidation, while the treatment of this fell disease is attempted more and more successfully. We do not know the cause, or causes of cancer, but we do certainly know how to 'cure' it, if only early opportunities are vouchsafed to us. While it must be acknowledged that a correct appraisal of etiology and pathology will greatly facilitate the rational treatment of the disease, it may sometimes happen that the mode of treatment might help in arriving at the cause of the disease.

In a large number of cases of schizophrenia and allied disorders, the course of events is one of progressive deterioration, though reports of spontaneous recovery are not unknown. Such spontaneous recovery almost corresponds to spontaneous regression of a cancerous growth, and should not influence our outlook on the ultimate deterioration. With such a grey outlook, operation appears to be the only mode of relief. To quote Freeman and Watts, "When concern over the future leads to indecision and blocking of action: when painful self-consciousness leads to apprehension and delusions of persecution: when perverted foresight raises up impenetrable barriers to happiness: and when, in contemplation, thoughts come into consciousness with the intensity of sound, then prefrontal lobotomy may provide a constructive mode of relief."

It would be rash to forecast the future of psychosurgery at this stage of development. We are still in the outer fringes of the knowledge of the mind, and time alone can decide whether this operation was correctly conceived and executed. But, this is certain that progress in the understanding of mental processes would receive a great stimulus. It is only necessary to recall the operation of complete colectomy for constipation, advocated by Sir Arbuthnot Lane. However inaccurately conceived, the operation paved the way for more accurate understanding of gastro-enterology. Similarly it would be a pardonable optimism to visualise a proper and scientific understanding of the functions and disorders of the frontal lobe following on the wake of this new phase of surgery, *viz.*, psychosurgery.

Summary

1. The history and development of psychosurgery has been traced from prehistoric times to the present day. 2. The theoretical basis of the operation is discussed. 3. The varieties and modifications of the operation are described. 4. The advantages of the operative method is contrasted with convulsion therapy. 5. The future of psychosurgery is surmised.

Acknowledgment

To Dr. V. V. Monteiro, Senior Surgeon with the Government of Mysore, my grateful thanks are due for his constant help and encouragement. It is with pleasure that I acknowledge the co-operation of my colleague Dr. M. V. Govindaswamy, Superintendent, Mental Hospital, Bangalore, where this work is

(*Continued at foot of col. 2, page 187*)

SPECIAL ARTICLE

THE CENTRAL DRUGS LABORATORY

A Plea for its Early Establishment

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The Drugs Act, 1940 (XXIII of 1940) received the assent of the Governor General on April 10, 1940 and Chapters I and II of the Act came into force at once. Chapter II deals with (1) The Drugs Technical Advisory Board, (2) The Central Drugs Laboratory and (3) The Drugs Consultative Committee.

The Drugs Act, though enacted hurriedly without giving the parties concerned sufficient time to suggest modifications to improve on the Bill, was welcomed by the medical profession in India as a measure, which, if properly applied and developed, may help to improve the condition of the drug industry in India so as to make India self-contained in its supply of pure and efficacious drugs at a cheap rate commensurate with the purchasing power of the poor disease-stricken people.

The Drugs Technical Advisory Board, when allowed to meet, at its very first meeting on November 3, 1942, "urged the Government to constitute the Central Drugs Laboratory at the earliest possible date, so that it may be in a position to begin the work which it is called upon to do under the Drugs Act, 1940". The Board again at its second meeting on March 14, 1944, discussed on the constitution of the proposed Laboratory, for the consideration of the Central Government, and passed the following resolutions:—

1. "The Board was of emphatic opinion that the Central Drugs Laboratory should be established at a very early date. It was suggested by Dr. Sen and the Board concurred with his suggestion that as the Provinces would have their own Laboratories in their capitals, it was advisable that the Central Drugs Laboratory with all its different sections should be located at one place, preferably in Delhi."

2. "It was also the opinion of the Board that the salaries provided should be sufficient to command the services of first class individuals and the status and emoluments of the personnel, grade for grade, of the various sections of the Central Drugs Laboratory should be the same."

Constitution of the Proposed Central Drugs Laboratory

I. *Director.* The Director should be a first class scientist and experienced administrator.

II. *Deputy Director.*

III. *Pharmaceutical Section:*—(*a*) Pharmaceutical Chemist—1, (*b*) Associate Chemist—1, (*c*) Assistant Chemists—3, (*d*) Associate Pharmacognocist—1, (*e*) Assistant Pharmacognocist—1.

IV. *Biochemical Section:*—(*a*) Biochemist—1, (*b*) Associate Biochemist—1, (*c*) Assistant Biochemist—1.

V. *Pharmacological Section:*—(*a*) Pharmacologist—1, (*b*) Associate Pharmacologist—1, (*c*) Assistant Pharmacologists—2.

VI. *Bacteriological Section:*—(*a*) Bacteriologist—1, (*b*) Associate Bacteriologist—1, (*c*) Assistant Bacteriologists—2 (one should be a Veterinary).

The Drugs Technical Advisory Board, when allowed to meet for the third time on the 26th January, 1945, once more adopted the following resolutions:—

(1) "The Board recalled that at its two previous meetings resolutions had been passed urging Government to establish the Central Drugs Laboratory at the earliest possible date. The Board considered that the Central Drugs Laboratory should be staffed and equipped to undertake all its functions and that it was undesirable to delegate a part of its functions to other laboratories as a permanent measure. The Board realises, however, that it would be a considerable time before the Central Drugs Laboratory would have accommodation, equipment and properly trained staff to undertake the efficient testing of the drugs specified in Schedule C, C(1), and C(2) necessitating work of a bacteriological or serological nature. The Board, therefore, recommended that until such time that a suitable section of the Central Drugs Laboratory has been established, work of this kind could be carried out at the Central Research Institute, Kasauli. Recognising the necessity for the Provincial Drugs Laboratories being modelled on the Central Drugs Laboratory, the Board wished to emphasize that the Central Government should inform the Provinces to this effect and should at the same time explain the reason for delegating a part of the functions of the Central Drugs Laboratory to the Central Research Institute, as an interim measure."

(2) The Board emphasizes the necessity for immediate action to set up the necessary government machinery to operate the Act in all areas before the Act comes into force.

In particular the Board again recommends that the Cenrtal Drugs Laboratory should be constituted forthwith and urges that the staff appointed to undertake the work of this very responsible Laboratory should be highly qualified and well paid so as to engender confidence in its efficient working among the general public and the various commercial interests concerned.

The functions of the Central Drugs Laboratory as laid down in the Drugs Rules, 1945, are:—(*i*) to analyse or test such samples of drugs as may be sent to it under sub-section (2) of section 11, or under sub-section (4) of section 25 of the Drugs Act, 1940; (*ii*) to grant certificates of registration in respect of patent or propietary medicines; (*iii*) to carry out such other duties as may be entrusted to it by the Central Government, by a Provincial Government, after consultation with the Drugs Technical Advisroy Board.

The duties under the above sub-section (3) as envisaged in the Report of the Drugs Enquiry Committee (Chopra Committee, 1930-31), Government of India, should be the following:—(*a*) to do research work on the pharmacological testing of drugs; (*b*) to train Public Analysts in the methods of chemical, bio-

chemical and biological assay; (*c*) to prepare and maintain stable standards of strength, purity and quality of drugs; (*d*) to standardize methods of analysis and tests with due regard to the climatic and other conditions prevailing in the different parts of India; (*e*) to periodically issue bulletins about its progress in various branches of its activities and supply information to manufacturers and Provincial Laboratories, as they may be in need of; and also to act as a National Centre for the preparation, maintenance, storage and distribution of international standards of therapeutic substances to different Drugs Laboratories and manufacturers.

The proper development of the pharmaceutical and drug industry on a sound and rational line greatly depends upon the confidence it is able to create in the medical profession and the public. Independent countries like U.K. and U.S.A., who place their country's interest above all other considerations, have developed their national drug industries on sound ethical lines by providing adequate legislations and facilities on behalf of the State to control and standardize their products. It is realised by all far-seeing and intelligent business executives and industrialists that standardization and quality control is one of the major clogs in the wheel of progress of the modern drug industry. The faith of India's citizens must first be created in the products manufactured in India and this can only be done by an unbiassed authoritative organisation, such as the proposed Central Drugs Laboratory, which would operate under the State auspices. If the seal of quality is put on Indian manufactured drugs by such an organization, the favourite bogey of the Government that Indian drugs are 'substandard' and therefore 'cheaper' than imported products would be removed once for all.

In India, the fact remains that, India is a mere dependency and not an independent nation. We are governed by foreigners whose main interest is the exploitation of the masses of our country for the commercial interest of their own country. Hence, though the Drugs Act was passed as early as April, 1940, and the nucleus of such a laboratory—the Bio-chemical Standardization Laboratory—is functioning since 1937, the alien Government of India have so far not taken any tangible step to establish the Central Drugs Laboratory, which is the first essential stage in implementing the Drugs Act, 1940. The Provincial Governments can then, and then only, establish their Provincial Laboratories, on the model of the Central Drugs Laboratory. The future of the national drug industry in India depends on the judicious enforcement of the Drugs Act, and the establishment of the Central and Provincial Drugs Laboratories on sound lines, which is, it seems, counter to the interest of the Government of India. The United Kingdom has, during the last war, fully developed its drug industries on a large scale, in Australia, in South Africa and in Canada. India is only to supply them with raw materials for their factories and is to remain for ever, as was in the past, the dumping ground for all those imported drugs. Such is apparently the policy of the Government of India, and hence its tardiness in implementing the Drugs Act, 1940. Our Legislatures should take a note of it for their future guidance—how the foreign personnel of their Executives are implementing their legislations. They have slept long enough and we should not permit them to do so any longer. The price that the country is paying for this neglect is too heavy than can be appreciated superficially.

(*Continued from page 185*)

conducted. My thanks are also due to the medical and nursing staff of the Mental Hospital.

REFERENCES

ACKERLEY, S.—*Am. J. Psychiat.*, **92**:717, 1935.
BALKRISHNA RAO, B. N. AND GOVINDASWAMY, M. V.—*Indian M. Gaz.*, **79**:212, 1944.
BETTANY, G. T.—'Eminent Doctors, their lives and their work' John Hogg, London. 1885.
BRICKNER, R. M.—*Arch. Neurol & Psychiat.*, **41**:580, 1939.
DAX, E. C. AND SMITH, E. J. R.—*J. Mental Sci.*, **89**: 182, 1943.
FREEMAN, W. AND WATT, J. W.—*Yale J. Biol and Med.*, **11**:527, 1939.
Idem—*J. Mental Sci.*, **90**:532, 1944.
FLEMING, G. W. T. H. AND MCKISSOCK, W.—*Lancet*, **1**:361, 1943.
GISSANE, W., BLAIR, D. AND RANK, B. K.—*Ibid.*, **1**:450, 1940.
GOLLA, F. L.—*J. Mental Sci.*, **89**:189, 1943.
GOVINDASWAMY, M. V.—*Lancet*, **1**:506, 1939
GRAY, H.—Text Book of Anatomy. Longmans, Green & Co. London. 1929.
HARVY GRAHAM—*Surgeons All. Rich and Cowan*, London. 1939.
HEBB, D. O. AND PENFIELD, W.—*Arch. Neurol & Psychiat.*, **44**:421, 1940.
HEMPHILL, R. E.—*Lancet*, **2**:152, 1942.
HORACE HILL—*Ibid.*, **2**:352, 1942.
HUTTON, E. L., FLEMING, G. W. T. H. AND FOX, F. E.—*Ibid.*, **2**:3, 1942.
JEFFERSON, G.—*Proc. Roy Soc. Med.*, **30**:851, 1937.
LYERLEY, J. G.—*J. Florida M. A.*, **25**:203, 1938.
MCGREGOR, J. S. AND CRUMBIE, J. R.—*Lancet*, **2**:7, 1941.
Idem—*Ibid.*, **1**:654, 1942.
MCKISSOCK, W.—*J. Mental Sci.*, **89**:194, 1943.
MEDUNA, L.—Die Konvulsionstherapie der Schizophrenie. Halle. 1937.
MONIZ, E.—Tentatives operatoires dans le traitment de certaines psychoses. Paris. 1936.
Idem—*Am. J. Psychiat.*, **93**:1379, 1937.
MOYNIHAN, SIR, B.—Addresses on Surgical Subjects. W. B. Saunders & Co. Philadelphia and London. 1928.
NICHOLS, I. C. AND HUNT, J. M.—*Am. J. Psychiat.*, **96**:1063, 1940.
O'BRIEN, J. D.—*J. A. M. A.*, **107**:657, 1936.
PAPEZ, J. W.—Comparative Neurology. T. Y. Crowell Co. New York. 1929.
PAVLOV, I. P.—Conditioned Reflexes. Oxford Univ. Press. London. 1927.
REES, T. P.—*J. Mental Sci.*, **89**:161, 1943.
SAKEL, M.—*Wien. med. Wochnschr*, **84**: 1211, 1265, 1299, 1326, 1353 & 1383, 1934.
SHEPLEY, W. H. AND MCGREGOR, J. S.—*Proc. Roy. Soc. Med.*, **33**:267, 1940.
STRECKER, E. A., PALMER, H. D. AND GRANT, F. D.—*Am. J. Psychiat.*, **98**:524, 1942.
STROM-OLSEN, R., LAST, S. L., BRODY, M. B. AND KNIGHT, G. C.—*J. Mental Sci.*, **89**:165, 1943.
WILLWAY, F. W.—*Ibid.*, **89**:192, 1943.
WOLTMAN, H. W., SMITH, B. F., MOERSCH, F. P. AND LOVE, J. G.—Proc. Staff Meet. Mayo Clinic., **16**:200, 1941.
WYLLIE, A. M.—*Lancet*, **2**:71, 1941.

CASE NOTES

PENICILLIN THERAPY IN MOFUSSIL

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Penicillin, has now come into civilian use in India. Its use, however, is mostly confined to big cities and places where frigidaires are available. Favourable reports of its use in Indian conditions recently appeared in the Indian medical press. But the practitioners and patients in mofussil stations are very greatly handicapped because of its high cost, elaborate technique of its use, and the extremely unstable nature of the product now marketed in India, namely, the sodium and calcium salt of penicillin. Very recently the writer started using penicillin in a few desperate cases without strictly adhering to the instructions regarding cold storage of penicillin. Results have been uniformly satisfactory. In most of these cases other drugs including sulphonamide preparations had been tried without any effect.

Previous experience of such cases pointed to an extremely grave prognosis. Where the patients' relatives could afford the price and were able to procure it from outside, penicillin was administered in the minimal doses of 100,000 Oxford units. Favourable reaction was seen immediately, even before the course was complete. Within about 24 hours the dangerous stage passed off. The subsequent process of complete resolution took a fairly long time.

Penicillin was mostly brought from Cuttack, about four hours' journey by rail, packed in ice when possible. Immediately on arrival here penicillin was dissolved in its original phial with 15 c.c. of sterilised distilled water. All measures for maintaining asepsis were taken during solution and administration of the drug. Intramuscular injections of 10,000 units were given every 4 hours. Lately we have given 15,000 units every three hours to increase and maintain blood concentration of penicillin and to utilise the solution quicker to anticipate further deterioration, whenever possible, the solution of the drug was kept in iced water but usually it was kept in magnesium sulphate solution. The syringe used was kept in sterile water and boiled in the same every time before use.

Subsequent to penicillin treatment usual routine treatment, local and general, was carried on as found appropriate to the existing conditions. After variable periods of after treatment all patients of this series were discharged cured.

Case Notes

Case 1—M.K. 27 M.M. the only son of a mofussil shopkeeper with previous history of gonorrhœal urethritis and unsuccessful treatment with M. & B. 693 was admitted with a fresh attack of urethritis with retention of urine and stool and flaccid paralysis of all four limbs. Urethral smear was positive to gonococci. The patient rallied round a bit with the usual routine treatment. M. & B. 693, 4 tablets a day was administered. With it there was an exacerbation in the patient's condition. In such a case, sulphapyridine intolerance pointed to a grave prognosis. At this stage penicillin was given at the instance of Captain A. P. Sinha, Civil Surgeon, Balasore. With 50,000 units the patient showed distinct improvement. With 100,000 units the septicæmic condition completely cleared up and localised into a periurethral abscess which was incised and drained. The patient had a long and slow convalescence.

Case 2—H.B. 26 M.F. admitted with extending cellulitis of face and mouth and high temperature. Sulphanilamide and sulphapyridine therapy stopped extension but no resolution appeared. Points of sloughy pus appeared here and there. General condition steadily deteriorated. The sloughing process extended. The patient was put on penicillin treatment. With 70,000 units there was great improvement and resolution was noticed. At this stage the patient left the hospital and was subsequently heard to have been cured.

Case 3—G.D. 38 H.F. admitted for erysipelas of the face including lips. Temperature 103°F, pulse 120. Treated outside with sulphanilamide. In hospital sulphathiazole treatment produced no effect. Penicillin was given on the 3rd day of admission and 11th day of the disease. With 50,000 units great improvement was noticed. With 100,000 units swelling disappeared and the part looked shrivelled up. Temperature dropped to 99°F. The patient subsequently had an eventful recovery with rapid resolution.

Case 4—B.C.M. 52 H.M. admitted with sloughing ulcer of the foot on the 15th day of disease. Pus smear showed short chained streptococci, staphylococci, diplococci and micrococcus tetragena. Afebrile. With 100,000 units of penicillin, the ulcer cleared up fully. During out-door treatment for this superficial ulcer he developed a tropical ulcer which is fairly common here. This was cured in due course with thiazamide acriflavin application.

Case 5—T.N. 30 M.F. pregnant, full term, admitted with sloughing cellulitis of lips and mouth, temperature 103°F, Mitral regurgitation and symptoms of heart failure. Pending the arrival of penicillin, sulphathiazole, 4 grams a day, was tried for 2 days with nicotinic acid and vitamin C tablets, glucose I.V. No effect. Penicillin was given on the 3rd day of admission and 10th day of the disease. With 100,000 units of penicillin temperature touched normal, resolution was noticed in the sloughing cellulitis which cleared up in another five days. The patient's heart condition continued to give anxiety. The patient had an easy delivery but a stormy puerperium. But she rallied round and was discharged cured on the 14th day after delivery.

Case 6—G.D. 58 H.F. a private case seen with sloughing cellulitis face—high temperature, very low general condition, delirium. Pending arrival of penicillin she was given cibazol, 2 tablets every four hours, glucose with strophanthin I.V.—no effect. Condition being serious 200,000 units of penicillin was obtained and administered. The patient had an uneventful and quick cure.

Conclusion

The purpose of this note is to show that penicillin can be used with advantage in mofussil stations even when frigidaires are not available. Inspite of a certain amount of deterioration due to faulty storage enough active penicillin was present to act favourably and to tide over the dangerous stage and save patients from sure death. It must, however, be stated that on the whole penicillin therapy in India is still not a practical proposition because of its prohibitive cost, elaborate technique and finally the very vexacious administration by too frequent injections for prolonged periods. Sooner or later this has to be superseded by an easier method and it is hoped that a stable salt of penicillin will soon be found. In this connection, Professor Bose's "Polyporin" opens up a new vista of renewed hope for the suffering humanity.

Acknowledgment

My thanks are due to Captain A. P. Sinha M.B., D.T.M., Civil Surgeon, Balasore, for having initiated the penicillin treatment at this place and for permission to publish this note.

References

Chatterjee, J. and De, M. N.—*J. Indian M. A.*, **14**:158, 1945.
Editorial—*Ibid.*, Penicillin and Sulphonamide, **14**:170, 1945.
Bose, S. R.—*Ibid.*, **14**:214, 1945.

USE OF PENICILLIN IN MULTIPLE VENEREAL INFECTIONS

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N. P., male, 35 years of age, cultivator, married, no children, came under observation on 2-8-45 for chronic gonorrhœal urethritis and he was referred to me by a doctor who treated him with two courses of sulphonamide compounds and with six injections of arsenic.

The patient had difficulty in micturition, duration 10 months and had ulceration on his pudenda also.

On examination I found phimosis, stricture urethra and pin-head-sized epitrochlear gland and he was provisionally diagnosed on 2-8-45 to be suffering from chancroid, syphilis and gonorrhœa. The diagnosis was confirmed by positive Ito-Reinsterna's test for chancroid, by positive blood Kahn *et al* and Wassermann reaction for syphilis and by the presence of few intra- and extracellular gram negative diplococci resembling *N. gonorrhœæ* in the prostatic smear examination which also showed the relationship between the pus to epithelial cells as 16:1. The urine showed on repeated examination presence of albumin in fair amount.

The patient was keen also to get the circumcision done for phimosis but I decided to give Penicillin therapy before doing the circumcision as the new drug is useful both for syphilis, gonorrhœa which is sulphonamide-fast and also for chancroid (Lahiri, 1945*a*).

Treatment

The patient was given penicillin dissolved in normal saline (20,000 units in 1 c.c.). On 14-8-45 at 8 A.M. the first injection of penicillin 30,000 units was given intramuscularly and the injections were repeated every four hours in doses of 15,000 units day and night for eight days and a total of 48 injections were given with a total dose of 735,000 units of penicillin. The only reaction the patient had was a febrile reaction after 9 hours and an hour after the second injection when the patient had a total of only 45,000 units of penicillin and on the second day the patient had itching sensation starting 36 hours after the starting of penicillin therapy and continued for about 10 hours which could be controlled by bromide (gr. 20) repeated four hourly for three doses (Lahiri, 1946). Patient felt from the third day to the eighth day a peculiar pain all over the body. The patient was kept in bed and the diet was normal except that the water intake was reduced to only 3 pints in 24 hours. Urine examination on the third day revealed no albumen and the prostatic smear examination daily showed improvement in the relationship between pus and epithelial cells and the gonococci disappeared when the first sample of prostatic smear was examined after 24 hours therapy. Blood W. R. negative after 2 weeks, after 10 weeks and on 18-12-45. Phimosis disappeared also.

Conclusion

For multiple infection of venereal origin the author strongly advocates penicillin therapy particularly in patients showing albuminuria. Chancroid is cured with penicillin (Lahiri, 1945*b*). In the modern treatment of syphilis the author (1945*c*) has advocated the judicious use of penicillin and in the Neisserian infection and its complications penicillin has been found to be of immense value (1945*d*). A control to penicillin therapy in venereal practice is recommended early otherwise penicillin-insensitive cases of syphilis, gonorrhœa and chancroid will be as common as the sulphonamide-fast cases due to improper doses in inexperienced hands and latent cases of all the different types of venereal diseases will increase in India thus making the control of V.D. all the more difficult.

References

Lahiri, K. D.—XXII All-India Medical Conference, 1945*a*.
Idem—Common Skin & Venereal Diseases of India. Himalaya Publication, Patna, E. I. Ry., 1945*b*.
Idem—Venereal Diseases & Modern Syphilotherapy. Himalaya Publication, Patna E. I. Ry., 1945*c*.
Idem—Antiseptic, 1945*d*.
Idem—Penicillin in V. D. in India. Himalaya Publication, Patna, E. I. Ry., 1946.

JOURNAL OF THE
INDIAN MEDICAL ASSOCIATION
CALCUTTA, MARCH, 1946

SIR U. N. BRAHMACHARI

Sir U. N. Brahmachari died at his home at Calcutta on February 6. History will recognise that the greatness of his life lay not in his individual scientific publications, his keen perception, profound erudition, but in his being the pioneer in a medical field, which was still then unrecognised by the practisers of healing art, *viz.*, chemotherapeutic research. Till his discovery of "urea stibamine", millions of people lost their lives due to kala-azar in various parts of India, specially, Assam and Bengal. Kala-azar was the forerunner of death and with the discovery of Sir U. N. came hope in millions of breasts and the scourge was conquered. Against untold odds, with no encouragement, no help and without any modern equipment, this pioneer worker worked day and night in a dingy room in the Campbell Medical School, Calcutta. His achievement blazed the trail of research in India.

His was a great life full of achievements and laurels, a life which was worth living for, a life which will remain before all of us as an example of service for which our profession stands.

May God give his soul peace and consolation to the bereaved family!

PHARMACY BILL*

After more than 2 to 3 decades of agitation, both inside the Assembly as well as outside, chiefly led by the members of the medical profession, the Government of India have ultimately seen their way to put up a Bill for the control of pharmacists, including the regulation of pharmaceutical education. Though the Bill cannot be said to have been perfectly drafted, there is no denying that this is one of the outstanding public health programmes put forward by Government this year. It appears from the preamble of the Bill that the Health Department of the Government of India have ultimately realised a truism which has been stressed in season and out of season by medical men and pharmacists that "compounding and dispensing of medicines by unqualified persons may endanger human life and that it is necessary to ensure that persons practising the profession of pharmacy should attain a satisfactory standard of education and training".

'Pharmacy' in the sense in which the term is used in western countries is almost non-existent in India, and, therefore, few medical men here realise the important part which the pharmacists play in matters regarding public health and medical practice. The pharmacists are the people who deal directly with drugs —they prepare, compound and dispense drugs, including potent remedies and dangerous poisons. The physician of to-day has no time at his disposal to dispense his own prescriptions and he must depend, to a very large extent, on the knowledge and efficiency of this class of workers in order to ensure the purity and potency of the drugs prescribed to his suffering patients. The relation of pharmacy to the practice of medicine in everyday life, therefore, is intimate, and consequently the pharmacists, like dentists and nurses, form an integral part of the health service (both preventive and curative) which centres round the medical man.

Pharmacy in India, as has been remarked in the Report of the Drugs Enquiry Committee of the Government of India (1930-31), is in a most deplorable condition in contrast with Great Britain, the Continent of Europe, United States of America and nearly all civilised countries of the world. The profession here, is represented by a class of people known as 'compounders', whose status, functions and duties are ill-defined and improperly understood. There appears to be no limit to their field of activity, though they are generally very poorly trained, even for their legitimate job of compounding, dispensing and serving remedies to the sick according to the prescriptions of the physicians. The 'compounders' are often found, particularly in the rural areas, engaged in duties, *e.g.*, that of a junior doctor, a hospital dresser, a laboratory and clinical assistant, anæsthetist, operation assistant, instrument clerk, etc., which their colleagues in western countries consider completely out of their purview. The inevitable result of this 'jack-of-all-trade' policy has been a low general standard of efficiency of the 'compounder' class as a whole. The high sense of professional prestige and ethical dealing in drugs of standard quality only, which characterise the pharmaceutical profession in western countries, have consequently not developed in India. It is, therefore, not surprising that members of the medical profession were one of the earliest to realise the need for better pharmaceutical training and have fought side by side with some of the early foreign trained pharmacists in this country for an improvement of the standard of this class of people. The realisation became particularly strong, when the medical profession had to face the widespread drug adulteration and spurious drug trade in India and they felt helpless to control the situation without the service of a qualified and ethical pharmaceutical profession.

In the Chairman's Address[1] before the All-India Pharmaceutical Conference held in Bombay in 1945 it has been stressed that pharmacy is a noble profession closely linked with medicine and should be brought up to the same high standard of efficiency as is present in Great Britain and America. In order to achieve this objective, the most important things that require immediate and drastic reorganisation are: (*i*) improvement of the educational qualifications and the raising of the status and pay of those who take up the pro-

* Elsewhere the 'Pharmacy Bill' (Gazette of India. Dec. 8, 1945) is being published *in extenso* for eliciting comments and suggestions for improvement by the interested readers.

[1] *Indian J. Pharmacy*, **1**:43, 1945.

fession of pharmacy and (*ii*) the enactment of a legislation preventing the practice of the profession of pharmacy by unqualified persons. As is well-known, the practice of pharmacy here is subject to no laws or restrictions whatsoever. The titles 'chemists', 'druggists', 'dispensing chemists', 'pharmaceutical chemists', 'pharmacists', etc., are freely used by anybody who might take a fancy for them. There is nothing to prevent the most ignorant person in the street from opening a drug shop and dispense the deadliest poisons to the unwary public.

By putting up the Bill for the control of pharmacy, the Central Government has taken a much overdue move in the right direction. The Bill seeks to create 'Central' and 'Provincial' Pharmaceutical Councils and to provide for the registration of pharmacists possessing a minimum qualification, which will be laid down by 'Education Regulations' made by the Central Pharmaceutical Council. The term 'compounder' will go forever and will be replaced by the more honourable designation of 'pharmacist'. In the initial stages, in addition to those possessing degrees in pharmacy of Indian or foreign Universities, people having qualifications, *e.g.*, (*a*) passing of an examination recognised as adequate by the Provincial Government for 'compounders' or 'dispensers' or (*b*) experience in the compounding of drugs in a hospital or dispensary or other place in which drugs are regularly dispensed on prescriptions of medical practitioners for a total period of not less than 5 years, will also be considered competent to be entered in the Register of Pharmacists. These classes will temporarily fill up the vacuum but would inevitably be weeded out, as legislation is enforced and pharmaceutical education progresses in its wake. If the Bill is given effect to immediately after it is approved in the Assembly, (not like the Drugs Act of 1940, which is still hibernating in the cold shelves of the Government archives),[1] pharmacy as a public health profession will arise in this country and will gradually make its beneficent influence felt. Pharmacy is an essential public service and without its constant help, scientific medical practice and honest drug trade cannot prosper.

[1] SEN, ANIL KUMAR—*J. Indian M. A.*, **15**:186, 1945.

(*Continued from page 193*)

2. Pyridoxine produces granulocytopoiesis by an effect on the myelocytic elements of the bone marrow. It seems probable that pyridoxine is the factor involved in the maturation and emigration of the polymorphonuclear leucocyte.

JAUNDICE IN AMOEBIC LIVER ABSCESS

REDDY AND RANGAM (*Indian M. Gaz.*, **80**:501, 1945) report from the Department of Pathology, Madras Medical College two cases of jaundice in tropical liver abscess with complete autopsy findings. These reports emphasize that in tropical countries hepatomegaly with jaundice should suggest the possibility of an amœbic abscess in common with other toxic, degenerative, inflammatory and neoplastic conditions. A routine examination of fæces for the vegetative and cystic forms of *Entamœba histolytica* is of paramount importance, since coincidental hepatic and colonic lesions are common. A diagnostic aspiration should be done unhesitatingly, since the material obtained can in any case be utilized for a histopathological examination to decide upon the nature of the malignant growth, if the material is not amœbic pus. The authors give the following explanation for the jaundice in amœbic liver-abscess: The sub-icteric tinge seen in amœbic hepatitis is due to the impaired function of the liver, the cause of toxic jaundice. But deep jaundice in both acute as well as long standing abscesses is produced differently. In an acute abscess with ragged walls the tension is not high to produce obstruction to the main bile ducts but it is the peri- and intra-ductal inflmmation which produces partial or complete obstruction; in a long standing abscess with thick fibrous wall the tension inside is high and pressure on the main bile duct should cause jaundice of an obstructive type. The occurrence of jaundice is primarily influenced by the situation of an abscess and the nature of its wall and least by its size and this would explain the absence of jaundice in abscesses which are very large but situated on the anterio-posterior aspect.

DIARRHOEA DUE TO GIARDIA LAMBLIA

FRASER (*Brit. M. J.*, **2**:184, 1945) writes that among 872 cases of diarrhoeal diseases treated in a British general hospital in India, *Giardia intestinalis* was the sole apparent cause in 21 and was present also in four cases of bacillary dysentery and in four of amœbic dysentery. All the 21 patients had diarrhœa and 15 complained of colic, which was relieved by evacuation of the bowels; tenesmus was present in one case only. In nearly all, the stools were watery faecal, rather paler than normal, and generally appeared greasy; in two cases blood and mucus were present. The duration of symptoms before admission to hospital varied from 1 to 35 days, but in most cases it was a few days only. Treatment with mepacrine—0·1 gm. t.d.s. for five days—cured all except two and a second course cured these. All the patients were given a generous diet and symptoms disappeared by the third day of treatment.

GIARDIASIS ASSOCIATED WITH RECURRENT RECTAL HAEMORRHAGES

HEMMING (*Brit. M. J.*, **2**:185, 1945) reports the following case of Giardiasis associated with rectal hæmorrhage:—

A female child, aged four years, was admitted to hospital at Suva, Fiji, on March 13, 1944, with a history of fever, constipation, weakness, and passage of blood with the stools. Physical examination revealed no abnormality, but she continued to pass blood until her discharge to the out-patient department on May. The blood passed was sometimes clotted, sometimes bright red, and mucus was often present. The stools were soft and pale and there was often diarrhœa. No parasites were found in the fæces and sigmoidoscopy showed no abnormality. Her blood contained 3,100,000 erythrocytes per c.mm. and hæmoglobin 80 per cent.

She was readmitted with the same symptoms six days later; examination of the stools on various dates showed infestation with *Trilhuris* and hookworm and, on May 27, a heavy infestation with *Giardia intestinalis*. On June 1 her blood showed 2,800,000 erythrocytes and hæmoglobin 60 per cent. Treatment was given for the anæmia, and mepacrine, ¾ grain t.d.s. for five days, was given for the giardiasis and was repeated after 10 days; no blood appeared in the stools after the first course of mepacrine and the patient was discharged on June 22.

CURRENT MEDICAL LITERATURE

Meningoccal Meningitis

Sweet and others (*An. Int. Med.*, **23**:338, 1945) write that they have treated 207 patients with meningococcic meningitis during a three year period, using either sulphadiazine or sulphamerazine as the principal therapeutic agent. The gross mortality was 10·1 per cent. There was no significant difference in the case fatality rate in patient treated with the two drugs.

The number of patients treated, the case fatality rate, and the duration and severity of illness were less in 1944 than in 1943.

The etilogic diagnosis was established immediately from direct examination of the cerebrospinal fluid in 188 (90·8 per cent) of this group of 207 patients.

The factors of the greatest prognostic significance at the time of admission were the presence or absence of the coma-delirium state and the age of the patient. In patients who were delirious or in coma, the finding of numerous micro-organisms in or the virtual absence of dextrose from the initial specimen of cerebrospinal fluid added to the gravity of the prognosis.

There was no relationship between the concentration of the sulphonamide in the blood and the outcome in meningitis. Massive doses of these drugs are not necessary for most patients with meningococcic meningitis. Careful appraisal of patients and of the findings in the cerebrospinal fluid will indicate those patients who require more vigorous treatment.

Lower Lung Field Tuberculosis

Romendick and others (*Dis. Chest.*, **10**:481, 1944) write that they studied the rœntgenograms of 2,354 consecutive patients with pulmonary tuberculosis discharged from the Robert Koch Hospital (St. Louis) from February 1933 to February 1942. Excluded from this study were upper lobe lesions and primary infections; also cases of bronchiectasis and pleural effusion or pleural thickening unless a parenchymal tuberculous lesion was also present. Sixty-three examples of lower lung field tuberculosis were found, an incidence of 2·7 per cent; 44 cases were in females and 19 in males; 43 patients were white and 20 Negroes. The ages ranged from fifteen to fifty-eight, with 49 patients (91·5 per cent) under forty. Among the Negroes, 90 per cent were under thirty; the oldest Negro was thirty-three years of age. There were 37 instances of right-side and 26 of left-side involvement; 24 patients had moderately advanced and 39 far advanced lesions. In onset, symptoms, duration, pathology, and prognosis, the disease differed in no way from the usual form of pulmonary tuberculosis.

Clinical Study of Sensitivity to Sulphathiazole

Kent and Diefendorf (*Am. J. M. Sc.*, **209**:640, 1945) write that of four hundred seventy-two patients who received a primary course of sulphathiazole therapy. one hundred ten developed some form of reaction to the drug. Of the one hundred ten reactions, forty-six were allergic in nature. Drug fever occurred in practically all cases showing any type of sensitivity reaction and was taken as an index of allergic response to the drug. The highest incidence of drug fever occurred on the ninth day of therapy. Of one hundred three patients receiving a second course of sulphathiazole after an interval of from two to one hundred eighty days, twenty-two manifested sensitivity reactions. In this group, drug fever developed by the second day in those cases who had had drug fever during the first course. However, 75 per cent of the patients with drug fever during the second course had had no reaction in the first course and none of these developed their fever before the ninth day from the time the second course was started. This marked resemblance to serum sickness suggests the allergic nature of drug sickness. Neither the absolute interval between courses nor the dosage has any influence on the production of sensitivity reactions.

Cholecystitis

Bullock (*Med. J. Australia*, July, 1945, Ref. *Medical World*, **63**:658, 1946) points out that the symptoms of gall-bladder trouble are generally referred to the stomach. Most frequently a flatulent dyspepsia occurs in the form of discomfort half an hour after food, relieved by the belching of wind, and more pronounced after certain foods, such as fats, pastries and vegetables. In other cases the gastric symptoms appear an hour or more after food as heart-burn and acid eructations. Pain is an important symptom in all cases of cholecystitis. It varies from a little discomfort after meals to severe pain referred to the right costal margin and round the lower right costal margin and round the lower right ribs to the lower angle of the scapula *via* the eighth dorsal nerve. In a small minority of cases the pain extends to the right iliac fossa and then simulates appendicitis or renal trouble and, in fact, the three conditions may co-exist. The pain may even be felt at the left side and so suggest cardiac trouble, and even angina pectoris.

Reactions to 10,000 Pooled Liquid Human Plasma Transeusions

Miller and Tisdall (*J.A.M.A.*, **128**:863, 1945) write that an analysis of 10,000 questionnaires concerning reactions following the use of pooled liquid human plasma revealed that thermal and allergic reactions were the ones most frequently encountered. Hæmolytic reactions were not noted after any of the transfusion. A careful cleansing of all apparatus tends to preevnt thermal reactions. In the 10,000 cases reviewed, there were a total of two hundred ninety-six reactions to which one hundred five (34·2 per cent) were of the allergic type. Of this number, one hundred two were urticarial and three were asthmatic. All responded satisfactorily to small doses of epinephrine. Three possible mechanisms which underlie these allergic reactions are: (1) transfer of food ingested by the donor, to which the recipient is sensitive, (2) passive transfer of sensitivity, and (3) sensitivity to common normal substances in the plasma. Although a small number of the allergic reactions can be avoided by proper selection of donors who should be on a semifasting diet for six hours previous to the blood donation, the majority which are due to the normal substances in the plasma, are unavoidable.

Medical Management of Jaundice

Steigmann and Papper (*Illinois M. J.*, **86**:164, 1944) write that except in hæmolytic jaundice, the pathologic changes in the liver cells of all other types of jaundice (including catarrhal, surgical infections, and toxic jaundice and the jaundice of cirrhosis, Weil's disease, and toxæmia of pregnancy) are fairly identical. The differences in these diseases appear to be a matter of degree of involvement rather than type of change.

High contents of liver glycogen are beneficial in withstanding toxic changes while fatty livers are not desirable. Fat in the diet should, therefore, be limited. Since high blood sugar levels must be attained before glycogen becomes deposited in the liver it is necessary that the carbohydrate intake be high. If necessary parenteral dextrose therapy is used.

High protein diets should be used since low blood protein levels tend to reduce wound healing and to favour œdema. However, meat is not the best protein to be used: amino acids are preferable and if necessary may be given parenterally.

Mineral intake is within normal range since mineral metabolism appears not to be disturbed. Fluids should be limited to control œdema but restriction should not be carried to the point of dehydration. Vitamins should be supplied abundantly. Choline has lipotropic action and its inclusion in the diet helps liver fat. Bile salts are employed when choleresis is desirable but of course are not used in obstructive jaundice. Since barbiturates are detoxified in the liver their use in liver damage should be avoided. Morphine and the sulphonamides are best not used because of their effect on the liver.

Treatment of Bronchiectasis

Thomas and others (*Ann. Int. Med.*, **23**:405, 1945) write that of 190 consecutive cases of bronchiectasis it was found that approximately one-half had major allergy of the respiratory tract. A clinical study was made of 75 selected cases of bronchiectasis to evaluate sulphonamide therapy and allergy management in treatment. In 55 of these cases an allergy of the respiratory tract was an eitologic or complicating factor.

Twenty-three cases received sulphonamide drugs as the chief or only therapeutic measure and were observed for four months to four years. Twenty-two of these patients showed definite improvement with reduction of cough and expectoration.

Twenty-one cases treated chiefly or wholly with allergy management were observed for a period of time ranging from one to four and one-half years. Fifteeen of this group showed frank improvement with reduction in cough and expectoration.

In 31 cases combined allergy and sulphonamide therapy was used. Twenty-six cases were found to have a least 25 to 100 per cent improvement in cough and expectoration. They were observed for six months to five years.

Recurrences of symptoms of original severity were frequently noted following acute respiratory infection, cessation of allergy management, or in some cases when infrequent courses of sulphonamide drugs were used.

Penicillin Treatment of Neurosyphilis

Rose and others (*Am. J. Syph. Gon. & Ven. Dis.*, **29**:487, 1945) write that during the twelve months ending Feb. 1, 1945, 106 patients with neurosyphilis were treated with penicillin. The great majority of patients were also given either malaria or fever cabinet therapy in approximately one-half the amount generally accepted as sufficient. Penicillin was administered intramuscularly in doses of 50,000 Oxford units per injection for a total of sixty injections (3 million units). The time interval of injection was varied according to a plan designed to give the maximum concentration. The over-all clinical and serologic results of seventy cases followed from four to twelve months form the basis of this report.

Clinically it is estimated that of these seventy cases, twenty-eight are improved, thirty-seven are unchanged and five are worse. The greatest percentage of improvement is to be found among the forty-nine cases diagnosed as general paresis. The most striking result, however, is shown in the six cases of primary optic atrophy, in five of which there may have been arrest of visual loss.

Spinal fluid examinations reveal an immediate response of an elevation in cells and total protein in most of the previously untreated patients, followed by a general gradual reduction in cell count, total protein and, later, a decrease in the Wassermann titer. Comparison between the clinical and serologic results shows no definite correlation at this stage of follow-up.

From the data presented it is believed that penicillin is an active and effective therapeutic agent for late neurosyphilis, but comparison with the serologic results of thirty patients treated by older methods indicates that there is no striking difference at this period of observation. Caution is advised in the interpretation of these results and we believe that the time has not arrived for the distribution of penicillin for general use in the treatment of neurosopyphilis.

Agranulocytic Angina Effectively Treated with Intravenous Pyridoxine Vitamin B_6)

Cantor and Scott (*Canadian M.A.J.*, **52**:368, 1945, Ref. *Indian M. Gaz.*, **80**:530, 1945) write that blood transfusions, so commonly used in this disorder, are described by Piney as useless and even dangerous. Pentose nucleotide has many advocates, but the dosage required, the long latent period before any improvement is noted, and its frequent ineffectiveness suggest that it is not a specific and that a remission might have occurred without its use.

Liver extract by the intravenous route is a more recent development. The clinical response to liver is difficult to assess because so often it has been combined with other measures. Experimentally, the reports are more promising.

It is thus clear that granulocytopenia in rats, which develops as a result of the administration of sulphonamides or thiourea, responds to liver or some liver extracts. Waisman and Elvehjem suggest that 'folic acid' is the active agent in this liver fraction. Daft and Sebrell provide experimental evidence for this view. In a critical review of this development, it is pointed out that the effect of folic acid may be indirect, in that folic acid is required by the coliform bacteria in the intestine for the production of some accessory substance which in turn produces the granulocytopoetic response.

Since pyroidoxine is a constitutent of liver and yeast, Vilter, Schiro and Spies administered pyridoxine intravenously to three pellagrins and two patents with pernicious anæmia in relapse. Improvment was noted within 48 hours, and although there was only a 5 per cent reticulocyte response, there was a striking increase in the leuccyte count, especially in the granulocytic series. Goldman and Malvados report somewhat similar observations in bone marrow studies on three cases of Cooley's anæmia. These findings led us to attempt the treatment of agranulocytic angina with intravenously administered pyridoxine.

The rapid and uniform response noted in our patient treated with pyridoxine hydrochloride intravenously (200 mg. daily) leads us to propose that:—

1. Pyridoxine is the factor in liver and liver extract responsible for the granulocytopoeitic effect noted when liver is administered in agranulocytic angina.

(*Continued at foot of page 191*)

PHARMACY BILL

S. H. OULSNAM

(To be introduced in the next session of the Central Legislative Assembly)

RESOLUTION

New Delhi, the 27th November, 1945

No. F. 45-144/45-H(I)—As the compounding and dispensing of medicines by unqualified persons may endanger human life it is necessary to ensure that persons practising the profession of pharmacy have attained a satisfactory standard of education and training. It is accordingly proposed to provide by legislation for the establishment of Pharmacy Councils, for the registration of pharmacists and for the regulation of the education of pharmacists. The Bill for this purpose, which it is proposed to introduce in the next session of the Legislative Assembly, is hereby published for general information.

A

BILL

to regulate the profession of pharmacy

Whereas it is expedient to make better provision for the regulation of the profession of pharmacy and for that purpose to constitute Pharmacy Councils;

It is hereby enacted as follows:—

CHAPTER I

INTRODUCTORY

1. *Short title, extent and commencement*—(1) This Act may be called the Pharmacy Act, 1945.

(2) It extends to the whole of British India.

(3) It shall come into force at once, but Chapters III, IV and V shall take effect in a particular Province only from such date as the Provincial Government may, by notification in the official Gazette, appoint in this behalf.

2. *Interpretation*—In this Act, unless there is anything repugnant in the subject or context,—

(*a*) "agreement" means an agreement entered into under section 20;

(*b*) "approved" means approved by the Central Council under section 12 or section 14;

(*c*) "British Indian University" means a university in British India established by an Indian law;

(*d*) "Central Council" means the Pharmacy Council of India constituted under section 3;

(*e*) "Executive Committeee" means the Executive Committee of the Central Council or of the Provincial Council, as the context may require;

(*f*) "medical practitioner" means a person holding a qualification granted by an authority specified in the Schedule to the Indian Medical Degrees Act, 1916 (VII of 1916) or in the Schedules to the Indian Medical Council Act, 1933 (XXVII of 1933);

(*g*) "prescribed" means in Chapter II prescribed by regulations made under section 18, and elsewhere prescribed by rules made under section 45;

(*h*) "Provincial Council" means a Provincial Council of Pharmacy constituted under section 19, and includes a Joint Provincial Council of Pharmacy constituted in accordance with an agreement under section 20;

(*i*) "register" means a register of pharmacists prepared and maintained under Chapter IV;

(*j*) "registered pharmacist" means a person whose name is for the time being entered on the register of the Province in which he is for the time being residing or carrying on his profession or business of pharmacy.

CHAPTER II

THE PHARMACY COUNCIL OF INDIA

3. *Constitution and composition of Central Council*—The Central Government shall, as soon as may be, constitute a Central Council consisting of the following members, namely:—

(*a*) six members, among whom there shall at all times be at least one teacher of each of the subjects, pharmaceutical chemistry, pharmacy and pharmacognosy, elected by the authority known as the Inter-University Board from among persons on the teaching staffs of British Indian Universities which grant a degree or diploma in pharmacy;

(*b*) five members, of whom at least three shall at all times be persons possessing a degree or diploma in pharmacy or pharmaceutical chemistry, nominated by the Central Government;

(*c*) one member elected by the Medical Council of India;

(*d*) the Director-General, Indian Medical Service, *ex-officio:*

Provided that if he is for any reason unable to be present at a meeting, he may in writing authorise a person to attend the meeting in his stead, and such person may take part in the discussions of the meeting but may not vote;

(*e*) the Director of the Central Drugs Laboratory, *ex-officio;*

(*f*) the Chief Chemist, Central Revenues, *ex-officio:*

(*g*) one member to represent each Governor's Province elected by the Provincial Council concerned:

Provided that for four years from the first constitution of the Central Council, in the stead of members elected under clause (*g*), each Government of the Governors' Provinces shall nominate one member, being a person eligible for registration as a pharmacist under section 31.

4. *Incorporation of Central Council*—The Council constituted under section 3 shall be a body corporate by the name of the Pharmacy Council of India, having perpetual succession and a common seal, with power to acquire and hold property both movable and immovable, and shall by the said name sue and be sued.

5. *President and Vice-President of Central Council*—(1) The President and Vice-President of the Central Council shall be elected by the members of the said Council from among themselves:

Provided that for four years from the first constitution of the Central Council the President shall be a person nominated by the Central Government who shall hold office at the pleasure of the Central Government and where he is not already a member, shall be a member of the Central Council in addition to the members referred to in section 3.

(2) An elected President or Vice-President shall hold office as such for a term not exceeding four years and not extending beyond the expiry of his term as member of the Central Council, but subject to his being a member of the Central Council, he shall be eligible for re-election.

6. *Mode of elections*—Elections under this Chapter shall be conducted in the prescribed manner, and where any dispute arises regarding any such election it shall be referred to the Central Government whose decision shall be final.

7. *Term of office and casual vacancies*—(1) Subject to the provisions of this section, a nominated or elected member other than a nominated President, shall hold office for a term of four years from the date of his nomination or election or until his successor has been duly nominated or elected, whichever is longer:

Provided that three of the members elected at the first election under clause (*a*) of section 3, two of the five members first nominated under clause (*b*) of that section and five of the members elected at the first election under clause (*g*) of that section (to be chosen in each case by lot under the supervision of the President and in such manner as he may decide) shall hold office for six years or until their respective successors have been duly elected or nominated, whichever is longer.

(2) A nominated or elected member may at any time resign his membership by writing under his hand addressed to the President, and the seat of such member shall thereupon become vacant.

(3) A nominated or elected member shall be deemed to have vacated his seat if he is absent without excuse sufficient in the opinion of the Central Council from three consecutive meetings of the Central Council.

(4) A casual vacancy in the Central Council shall be filled by fresh nomination or election, as the case may be, and the person nominated or elected to fill the vacancy shall hold office only for the remainder of the term for which the member whose place he takes was nominated or elected.

(5) No act by the Central Council shall be called in question on the ground merely of the existence of any vacancy in, or any defect in the constitution of, the Central Council.

(6) Members of the Central Council shall be eligible for renomination or relection.

8. *Staff, remuneration and allowance*—(1) The Central Council may appoint a Secretary who may also, if deemed expedient, act as Treasurer.

(2) The Central Council may, with the previous sanction of the Central Government,—

(*a*) appoint such other officers and servants as may be required to enable the Central Council to carry out its functions under this Act;

(*b*) fix the salaries and allowances and other conditions of service of the Secretary and other officers and servants;

(*c*) fix the rates of allowances payable to members of the Central Council.

9. *The Executive Committee.*—(1) The Central Council shall, as soon as may be, constitute an Executive Committee consisting of the President (who shall be Chairman of the Executive Committee) and Vice-President, *ex-officio,* and five other members elected by the Central Council from among its members.

(2) A member of the Executive Committee shall hold office as such until the expiry of his term of office as member of the Central Council, but, subject to his being a member of the Central Council, he shall be eligible for re-election.

(3) In addition to the powers and duties conferred and imposed upon it by this Act the Executive Committee shall exercise and discharge such powers and duties as may be prescribed.

10. *Education Regulations*—(1) Subject to the provisions of this section, the Central Council may make regulations, to be called the Education Regulations, prescribing the minimum standard of education required for qualification as a pharmacist.

(2) In particular and without prejudice to the generality of the foregoing power, the Education Regulations may prescribe—

(*a*) the nature and period of study and of practical training to be undertaken before admission to an examination;

(*b*) the equipment and facilities to be provided for students undergoing approved courses of study;

(*c*) the subjects of examinations and the standards therein to be attained:

(*d*) any other conditions of admission to examinations.

(c) Copies of the draft of the Education Regulations and of all subsequent amendments thereof shall be furnished by the Central Council to the Central Government and all Provincial Governments, and the Central Council shall before publishing the Education Regulations or any amendment thereof, as the case may be, take into consideration any comments of the Central Government or any Provincial Government received within three months from the furnishing of the copies as aforesaid.

(4) The Education Regulations shall be published in the official Gazette and in such other manner as the Central Council may direct.

(5) The Executive Committee shall from time to time report to the Central Council on the efficacy of the Education Regulations and may recommend to the Central Council such amendments thereof as it may think fit.

11. *Application of Education Regulations to Provinces*—At any time after the constitution of the Provincial Council under Chapter III and after consultation with the Provincial Council, the Provincial Government may, by notification in the official Gazette, declare that the Education Regulations shall take effect in the Province:

Provided that where no such declaration has been made, the Education Regulations shall take effect in the Province on the expiry of three years from the date of the constitution of the Provincial Council, unless the Provincial Government, by notification in the official Gazette, postpones such taking effect for such period, not exceeding two years at any one time, as may be specified in the notification.

12. *Approved coourses of study and examinations*—(1) Any authority in British India which conducts a course of study for pharmacists may apply to the Central Council, where after such inquiry as it may think fit to make, it is satisfied that the said course of study is in conformity with the Education Regulations, shall declare the said course of study to be an approved course of study for the purpose of admission to an approved examination for pharmacists.

(2) Any authority in British India which holds an examination in pharmacy may apply to the Central Council for approval of the examination, and the Central Council, where after such inquiry as it may think fit to make, it is satisfied that the said examination is in conformity with the Education Regulations, shall declare the said examination to be an approved examination for the purpose of qualifying for registration as a pharmacist under this Act.

13. *Withdrawal of Approval*—(1) Where the Executive Committee reports to the Central Council that an approved course of study or an approved examination does not continue to be in conformity with the Education Regulations, the Central Council shall give notice to the authority concerned of its intention to take into consideration the question of withdrawing the declaration of approval accorded to the course of study or examination, as the case may be, and the said authority may within three months from the receipt of such notice forward

to the Central Council through the Provincial Government such representation in the matter as it may wish to make.

(2) After considering any representation which may be received from the authority concerned and any obesrvations thereon which the Provincial Government may think fit to make, the Council may declare that the course of study or the examination shall be deemed to be approved only when completed or passed, as the case may be, before a specified date.

14. *Qualifications granted outside British India*—The Central Council, if it is satisfied that any qualification in pharmacy granted by an authority outside British India affords a sufficient guarantee of the requisite skill and knowledge, may declare such qualification to be an approved qualification for the purpose of qualifying for registration under this Act, and may for reasons appearing to it sufficient at any time declare that such qualification shall be deemed to be approved only when granted before a specified date.

15. *Mode of declarations*—All declarations under section 12, section 13 or section 14 shall be made by resolution passed at a meeting of the Central Council, and shall forthwith be published in the official Gazette.

16. *Inspection*—(1) The Executive Committee may appoint such number of Inspectors as it may deem requisite for the purposes of this Chapter.

(2) An Inspector may—

(*a*) inspect any institution which provides an approved course of study;

(*b*) attend at any approved examination;

(*c*) inspect any institution whose authorities have applied for the approval of its course of study or examination under this Chapter, and attend at any examination of such institution.

(3) An Inspector attending at any examination under sub-section (2) shall not interfere with the conduct of the examination, but he shall report to the Exectuive Committee on the sufficiency of every examination he attends and on any other matter in regard to which the Executive Committee may require him to report.

(4) The Executive Committee shall forward a copy of every such report to the authority concerned, and shall also forward a copy together with any comments thereon which the said authority may have made, to the Central Government.

17. *Information to be furnished*—(1) The Central Council shall furnish copies of its minutes and of the minutes of the Executive Committee and an annual report its activities together with an abstract of its accounts to the Central Government.

(2) The Central Government may publish in such manner as it may think fit any report, copy or abstract furnished to it under this section or under section 16.

18. *Power to make regulations*—(1) The Central Council may make regulations consistent with this Act to carry out the purposes of this Chapter.

(2) In particular and without prejudice to the generality of the foregoing power, such regulations may provide—for—

(*a*) the management of the property of the Central Council and the maintenance and audit of its accounts;

(*b*) the manner in which elections under this Chapter shall be conducted;

(*c*) the summoning and holding of meetings of the Central Council, the times and places at which such meetings shall be held, the conduct of business thereat and the number of members necessary to constitute a quorum;

(*d*) the functions of the Executive Committee, the summoning and holding meetings thereof, the times and places at which such meetings shall be held, and the number of members necessary to constitute a quorum;

(*e*) the powers and duties of the President and Vice-President;

(*f*) the tenure of office and the powers and duties of the Secretary, Inspectors and other officers and servants of the Central Council, including the amount and nature of the security to be furnished by the Treasurer.

(3) Until regulations are made by the Central Council under this section, the President may, with the previous sanction of the Central Government, make such regulations under this section, including those to provide for the manner in which the first elections to the Central Council shall be conducted, as may be necessary for carrying into effect the provisions of this Chapter; and any regulations so made may be altered or rescinded by the Central Council in exercise of its powers under this section.

CHAPTER III

Provincial Pharmacy Councils

19. *Constitution and composition of Provincial Councils*—Except where a Joint Provincial Council is constituted in accordance with an agreement made under section 20, the Provincial Government shall constitute a Provincial Council consisting of the following members, namely:—

(*a*) six members, elected from among themselves by registered pharmacists of the Province.

(*b*) five members, of whom at least two shall at all times be persons possessing a prescribed degree or diploma in pharmacy or pharmaceutical chemistry or members of the pharmaceutical profession, nominated by the Provincial Government;

(*c*) one member, elected by the Medical Council (by whatever name called) of the Province;

(*d*) the chief administrative medical officer of the Province, *ex-officio;*

Provided that if he is for any reason unable to be present at a meeting, he may in writing authorise a person to attend the meeting in his stead, and such person may take part in the discussions of the meeting but may not vote,

(*e*) the Government Analyst under the Drugs Act, 1940 (XXIII of 1940), *ex-officio*, or where there is more than one, such one as the Provincial Government may appoint in this behalf:

Provided that where an agreement is made under clause (*b*) of sub-section (1) of section 20, the agreement may provide that the Provincial Council to serve the needs of the other participating Provinces also shall be augmented by not more than two members, of whom at least one shall at all times be a person possessing a prescribed degree or diploma in pharmacy or pharmaceutical chemistry or a member of the pharmaceutical profession, nominated by the Governments of each of the said other participating Provinces, and where the agreement so provides, the composition of the Provincial Council shall be deemed to be augmented accordingly.

20. *Interprovincial agreements*—(1) Two or more provincial Governments may enter into an agreement to be in force for such period and to be subject to renewal for such further periods, if any, as may be specified in the agreement, to provide—

(*a*) for the constitution of a Joint Provincial Council for all the participating Provinces, or

(*b*) that the Provincial Council of one Province shall serve the needs of the other participating Provinces.

(2) In addition to such matters as are in this Act specified, an agreement under this section may—

(*a*) provide for the apportionment between the participating Provinces of the expenditure in connection with the Provincial Council or Joint Provincial Council;

(*b*) determine which of the particpating Provincial Governments shall exercise the several functions of the Provincial Government under this Act, and the references in this Act to the Provincial Government shall be construed accordingly;

(*c*) provide for consultation between the participating Provincial Governments either generally or with reference to particular matters arising under this Act;

(*d*) make such incidental and ancillary provisions, not inconsistent with this Act, as may be deemed necessary or expedient for giving effect to the agreement.

(3) An agreement under this section shall be published in the official Gazettes of the participating Provinces.

21. *Composition of Joint Provincial Councils.*—A Joint Provincial Council shall consist of the following members, namely:—

(*a*) such number of members, being not less than three and not more than five as the agreement shall provide, elected from among themselves by the registered pharmacists of each of the participating Provinces:

(*b*) such number of members, being not less than two and not more than four as the agreement shall provide, nominated by each participating Provincial Government;

(*c*) one member elected by the Medical Council (by whatever name called) of each participating Province;

(*d*) the chief administrative medical officer of each participating Province, *ex-officio:*

Provided that, if any such officer is for any reason unable to be present at a meeting, he may in writing authorise a person to attend the meeting in his stead, and such person may take part in the discussions of the meeting but may not vote;

(*e*) the Government Analyst under the Drugs Act, 1940 (XXIII of 1940) of each participating Province, *ex-officio.*

or where there is more than one in any such Province, such one as the Provincial Government may appoint in this behalf.

(2) The agreement may provide that within the limits specified in clauses (*a*) and (*b*) of sub-section (1), the number of members to be elected or nominated under those clauses may or may not be the same in respect of each participating Province.

(3) Of the members nominated by each Provincial Government under clause (*b*) of sub-section (1), at least half shall at all times be persons possessing a prescribed degree or diploma in pharmacy or pharmaceutical chemistry or members of the pharmaceutical profession.

22. *Incorporation of Provincial Councils*—Every Provincial Council shall be a body corporate by such name as may be notified by the Provincial Government in the official Gazette or, in the case of a Joint Provincial Council, as may be determined in the agreement, having perpetual succession and a common seal, with power to acquire or hold property both movable and immmovable, and shall by the said name sue and be sued.

23. *President and Vice-President of Provincial Council*—(1) The President and Vice-President of the Provincial Council shall be elected by the members from among themselves:

Provided that for four years from the first constitution of the Provincial Council the President shall be a person nominated by the Provincial Government who shall hold office at the pleasure of the Provincial Government and where he is not already a member, shall be a member of the Provincial Council in addition to the members referred to in section 19 or section 21, as the case may be.

(2) An elected President or Vice-President shall hold office as such for a term not exceeding four years and not extending beyond the expiry of his term as a member of the Provincial Council, but subject to his being a member of the Provincial Council, he shall be eligible for re-election.

24. *Mode of elections*—Elections under this Chapter shall be conducted in the prescribed manner, and where any dispute arises regarding any such election, it shall be referred to the Provincial Government whose decision shall be final.

25. *Term of office and casual vacancies*—(1) Subject to the provisions of this section, a nominated or elected member, other than a nominated President, shall hold office for a term of four years from the date of his nomination or election or until his successor has been duly nominated or elected, whichever is longer.

Provided that three of the members elected at the first election under clause (*a*) of section 19, two of the members nominated on the first constitution of the Provincial Council under clause (*b*) of that section, half of the number of members nominated on the first constitution of the Provincial Council under the proviso to the said section, half of the number of members elected at the first election under clause (*a*) of sub-section (1) of section 21 and half of the number of members nominated on the first constitution of a Joint Provincial Council under clause (*b*) of that sub-section (to be chosen in each case by lot under the supervision of the President and in such manner as he may decide) shall hold office for six years or until their respective successors have been duly elected or nominated, whichever is longer.

Explanation—The expression "half" in the proviso to this sub-section means in relation to an odd number the whole number next below the arithmetical half of such odd number.

(2) A nominated or elected member may at any time resign his membership by writing under his hand addressed to the President, and the seat of such member shall thereupon become vacant.

(3) A nominated or elected member shall be deemed to have vacated his seat if he is absent without excuse sufficient in the opinion of the Provincial Council from three consecutive meetings of the Provincial Council.

(4) A casual vacancy in the Provincial Council shall be filled by fresh nomination or election, as the case may be, and the person nominated or elected to fill the vacancy shall hold office only for the remainder of the term for which the member whose place he takes was nominated or elected.

(5) No act done by the Provincial Council shall be called in question on the ground merely of the existence of any vacancy in, or any defect in the constitution of, the Provincial Council.

(6) Members of the Provincial Council shall be eligible for renomination or re-election.

26. *Staff, remuneration and allowances*—The Provincial Council may, with the previous sanction of the Provincial Government,—

(*a*) appoint a Registrar who shall also act as Secretary and, if deemed expedient, Treasurer, of the Provincial Council;

(*b*) appoint such other officers and servants as may be required to enable the Provincial Council to carry out its functions under this Act;

(*c*) fix the salaries and allowances and other conditions of service of the secretary and other officers and servants of the Provincial Council;

(*d*) fix the rates of allowances payable to members of the Provincial Council.

27. *The Executive Committee*—(1) The Provincial Council shall as soon as may be, constitute an Executive Committee consisting of the President (who shall be Chairman of the Executive Committee) and Vice-President, *ex-officio*, and such number of other members elected by the Provincial Council from among themselves as may be prescribed.

(2) A member of the Executive Committee shall hold office as such until the expiry of his term of office as member of the Provincial Council, but, subject to his being a member of the Provincial Council, he shall be eligible for re-election.

(3) In addition to the powers and duties conferred and imposed upon it by this Act, the Executive Committee shall exercise and discharge such powers and duties as may be prescribed.

28. *Information to be furnished*—(1) The Provincial Council shall furnish such reports, copies of its minutes and of the minutes of the Executive Committee, and abstracts of its accounts to the Provincial Government as the Provincial Government may from time to time require.

(2) The Provincial Government may publish, in such manner as it may think fit, any report, copy, abstract or other information furnished to it under this section.

CHAPTER IV

Registration of Pharmacists

29. *Preparation and maintenance of register*—(1) As soon as may be after this Chapter has taken effect in any Province, the Provincial Government shall cause to be prepared in the manner hereinafter provided a register of pharmacists for the Province.

(2) The Provincial Council shall upon its constitution assume the duty of maintaining the register in accordance with the provisions of this Act.

(3) The register shall include the following particulars, namely:—

(*a*) the full name and residential address of the registered person;

(*b*) the date of his first admission to the register;

(*c*) his qualifications for registration;

(*d*) his professional address, and if he is employed by any person, the name of such person;

(*e*) such further particulars as may be prescribed.

30. *Preparation of first register*—(1) For the purpose of preparing the first register, the Provincial Government shall by notification in the official Gazette constitute a Registration Tribunal consisting of three persons, and shall also appoint a Registrar who shall act as Secretary of the Registration Tribunal.

(2) The Provincial Government shall, by the same or like notification, appoint a date on or before which applications for registration, which shall be accompanied by the prescribed fee, shall be made to the Registration Tribunal.

(3) The Registration Tribunal shall examine every application received on or before the appointed date, and if it is satisfied that the applicant is qualified for registration under section 31, shall direct the entry of the name of the applicant on the register.

(4) The first register so prepared shall thereafter be published in such manner as the Provincial Government may direct, and any person aggrieved by a decision of the Registration Tribunal expressed or implied in the register as so published may, within thirty days from the date of such publication, appeal to an authority appointed by the Provincial Government in this behalf by notification in the official Gazette.

(5) The Registrar shall amend the register in accordance with the decisions of the authority appointed under sub-section (4) and shall thereupon issue to every person whose name is entered on the register a certificate of registration in the prescribed form.

(6) Upon the constitution of the Provincial Council, the register shall be given into its custody, and the Provincial Government may direct that all or any specified part of the application fees for registration in the first register shall be paid to the credit of the Provincial Council.

31. *Qualifications for entry on first register*—A person shall be entitled on payment of the prescribed fee to have his name entered on the first register if he resides, or carries on the business or profession of pharmacy, in the Province and if he—

(*a*) holds a degree or diploma in pharmacy or pharmaceutical chemistry of a British Indian University or a prescribed qualification granted by an authority outside British India, or

(*b*) holds a degree of a British Indian University other than a degree in pharmacy or pharmaceutical chemistry, and has been engaged in the compounding of drugs in a hospital or dispensary or other place in which drugs are regularly dispensed on prescriptions of medical practitioners for a total period of not less than three years, or

(*c*) has passed an examination recognised as adequate by the Provincial Government for compounders of dispensers, or

(*d*) has been engaged in the compounding of drugs in a hospital or dispensary or other place in which drugs are regularly dispensed on prescriptions of medical pracitioners for a total period of not less than five years.

32. *Qualifications for subsequent registration*—(1) After the date appointed under sub-section (2) of section 30 and before the Education Regulations have, by or under section 11, taken effect in the Province, a person shall on payment of the prescribed fee be entitled to have his name entered on the register if he resides or carries on the business or profession of pharmacy in the Province and if he—

(*a*) satisfies the prescribed conditions, or where no conditions have been prescribed, the conditions entitling a person to have his name entered on the first register as set out in section 31, or

(*b*) is a registered pharmacist in another Province, or

(*c*) possesses a qualification approved under section 14:

Provided that no person shall be entitled under this sub-section to have his name entered on the register unless he has passed a matriculation examination or an examination prescribed as being equivalent to a matriculation examination.

(2) After the Education Regulations have by or under section 11 taken effect in the Province, a person shall on payment of the prescribed fee be entitled to have his name entered on the register if he has attained the age of twenty-one

years, if he resides, or carries on the business or profession of pharmacy, in the Province and if he has passed an approved examination or possesses a qualification approved under section 14.,

33. *Scrutiny of applications for registration*—(1) After the date apponted under sub-section (2) of section 30, applicants for registration shall be addressed to the Registrar of the Provincial Council and shall be accompanied by the prescribed fee.

(2) If upon such application the Registrar is of opinion that the applicant is entitled to have his name entered on the register under the provisions of this Act for the time being applicable, he shall enter the name of the applicant on the register:

Provided that no person whose name has under the provisions of this Act been removed from the register of any Province shall be entitled to have his name entered on the register except with the approval of the Provincial Council recorded at a meeting.

(3) Any person whose application for registration is rejected by the Registrar, may within three months from the date of such rejection appeal to the Provincial Council, and the decision of the Provincial Council thereon shall be final.

(4) Upon entry on the register of a name under this section, the Registrar shall issue a certificate of registration in the prescribed form.

34. *Renewal fees*—(1) The Provincial Government may, by notification in the official Gazette, direct that for the retention of a name on the register after the 31st day of December of the year following the year in which the name is first entered on the register, there shall be paid annually to the Provincial Council such renewal fee as may be prescribed and where such direction has been made, such renewal fee shall be due to be paid before the first day of April of the year to which it relates.

(2) Where a renewal fee is not paid before the due date, the Registrar shall remove the name of the defaulter from the register.

Provided that a name so removed may be restored to the register on payment, at any time during the remaining nine months of the year, of double the renewal fee prescribed.

(3) On payment of the renewal fee, the Registrar shall in the prescribed manner endorse the certificate of registration accordingly.

(4) A person whose name is removed from the register under sub-section (2) and not restored thereto under the proviso to that sub-section, shall not be entitled to be again registered except with the approval of the Provincial Council and on such conditions as to payment of fees as it may direct.

35. *Entry of additional qualifications*—A registered pharmacist shall on payment of the prescribed fee be entitled to have entered in the register any further degrees or diplomas in pharmacy or pharmaceutical chemistry which he may obtain.

36. *Removal from register*—(1) Subject to the provisions of this section, the Executive Committee may order that the name of a registered pharmacist shall be removed from the register, where it is satisfied, after giving him, a reasonable opportunity of being heard and after such further inquiry, if any, as it may think fit to make,—

(*i*) that his name has been entered on the register in error or on account of misrepresentation or suppression of a material fact, or

(*ii*) that he has been convicted of any such offence or has been guilty of any such misconduct as in the opinion of the Executive Committee renders him unfit to be a registered pharmacist, or

(*iii*) that a person employed by him for the purposes of his business of pharmacy has been convicted of any such offence or has been guilty of any such misconduct as would, if such person were a registered pharmacist, render him liable to have his name removed from the register under clause (*ii*):

Provided that no such order shall be made under clause (*iii*) unless the Executive Committee is satisfied—

(*a*) that the offence or misconduct was instigated or connived at by the registered pharmacist, or

(*b*) that the registered pharmacist has at any time during the period of twelve months immediately preceding the date on which the offence or misconduct took place, committed a similar offence or been guilty of similar misconduct, or

(*c*) that any person employed by the registered pharmacist for the purposes of his business of pharmacy has at any time during the period of twelve months immediately preceding the date on which the offence or misconduct took place, committed a similar offence or been guilty of similar misconduct, and that the registered pharmacist had, or reasonably ought to have had, knowledge of such previous offence or misconduct, or

(*d*) that where the offence or misconduct continued over a period, the registered pharmacist had, or reasonably ought to have had, knowledge of the continuing offence or misconduct, or

(*e*) that where the offence is an offence under the Drugs Act, 1940 (XXIII of 1940), the registered pharmacist has not used due diligence in enforcing compliance with the provisions of that Act in his place of business and by persons employed by him.

(2) An order under sub-section (1) may direct that the person whose name is ordered to be removed from the register shall be ineligible for registration in the Province under this Act either permanently or for such period of years as may specified.

(3) An order under sub-section (1) shall be subject to the confirmation by the Provincial Council and shall not take effect until the expiry of three months from the date of such confirmation.

(4) A person aggrieved by an order under sub-section (1) which has been confirmed by the Provincial Council may, within thirty days from the communication to him of such confirmation, appeal to the Provincial Government, and the order of the Provincial Government upon such appeal shall be final.

(5) A person whose name has been removed from the register under this section or under sub-section (2) of section 34 shall forthwith surrender his certificate of registration to the Registrar, and names so removed shall be published in the official Gazette.

37. *Restoration to register*—The Executive Committee may at any time for reasons appearing to it sufficient order that upon payment of the prescribed fee the name of a person removed from the register shall be restored thereto.

Provided that where an appeal against such removal has been rejected by the Provincial Government, an order under

this section shall not take effect until it has been confirmed by the Provincial Council.

38. *Bar of other jurisdiction*—No order refusing to enter a name on the register or removing a name from the register shall be called in question otherwise than in the manner provided in this Act.

39. *Issue of duplicate certificates of registration*—Where it is shown to the satisfaction of the Registrar that a certificate of registration has been lost or destroyed, the Registrar may, on payment of the prescribed fee, issue a duplicate certificate in the prescribed form.

40. *Printing of register*—As soon as may be after the first day of April in each year, the Registrar shall cause to be printed copies of the register as it stod on the said date, and such copies shall be made available to persons applying therefor on payment of the prescribed charge and shall be evidence that on the said date the persons whose names are entered therein were registered pharmacists.

CHAPTER V

MISCELLANEOUS

41. *Penalty for falsely claiming to be registered*—(1) If any pereson whose name is not for the time being entered on the register of the Province falsely pretends that it is so entered or uses in connection with his name or title any words or letters reasonably calculated to suggest that his name is so entered, he shall be punishable with fine which may extend to five hundred rupees:

Provided that it shall be a defence to show that the name of the accused is entered on the register of another Province and that at the time of the alleged offence under this section an application for registration in the Province had been made.

(2) For the purposes of this section—

(*a*) it shall be immaterial whether or not any person is deceived by such pretence or use as aforesaid;

(*b*) the use of the description "pharmacist" shall be deemed to be reasonably calculated to suggest that the user is a person whose name is for the time being entered on the register of the Province;

(*c*) the onus of proving that the name of a person is for the time being entered on the register of a Province shall be on him who asserts it.

(3) Cognizance of an offence punishable under this section shall not be taken except upon complaint made by order of the Provincial Government or the Executive Committee.

42. *Dispensing by unregistered persons*—(1) On or after such date as the Provincial Government may by notification in the official Gazette appoint in this behalf, no person other than a registered pharmacist shall compound, prepare, mix, or dispense any medicine on the prescription of a medical practitioner except under the direct and personal supervision of a registered pharmacist:

Provided that this sub-section shall not apply to the dispensing by a medical practitioner of medicine for his own patients, or with the general or special sanction of the Provincial Government, for the patients of another medical practitioner.

(2) Whoever contravenes the provisions of sub-section (1) shall be punishable with simple imprisonment for a term which may extend to six months, or with fine or with both.

(3) Cognizance of an offence punishable under this section shall not be taken except upon complaint made by an order of the Provincial Government.

43. *Failure to surrender certificate of registration*—(1) If any person whose name has been removed from the register fails without sufficient cause forthwith to surrender his certificate of registration, he shall be punishable with fine which may extend to fifty rupees.

(2) Cognizance of an offence punishable under this section shall not be taken except upon complaint made by an order of the Executive Committee.

44. *Payment of part of fes to Central Council*—The Provincial Council shall before the end of June in each year pay to the Central Council a sum equivalent to one-sixth (or such other proportion as may from time to time be agreed upon by the Central Council and the Provincial Government) of the total fees realised by the Provincial Council under this Act during the period of twelve months ending on the 31st day of March of that year.

45. *Power to make rules*—(1) The Provincial Government may, by notification in the official Gazette, make rules to carry out the purposes of Chapters III, IV and V.

(2) In particular and without prejudice to the generality of the foregoing power such rules may provide for—

(*a*) the management of the property of the Provincial Council, and the maintenance and audit of its accounts;

(*c*) the summoning and holding of meetings of the Provincial Council, the times and places at which such meetings shall be held, the conduct of business thereat and the number of members necessary to form a quorum;

(*d*) the powers and duties of the President and Vice-President of the Provincial Council;

(*e*) the constitution and functions of the Executive Committee, the summoning and holding of meetings thereof, the time and places at which such meetings shall be held, and the number of members necessary to constitute a quorum;

(*f*) the tenure of office and the powers and duties of the Registrar and other officers and servants of the Provincial Council, including the amount and nature of the security to be given by the Treasurer;

(*g*) the particulars to be stated, and the proof of qualifications to be given, in applications for registration under sub-section (1) of section 32;

(*i*) fees payable under Chapter IV and the charge for supplying copies of the register;

(*j*) the form of certificates of registration and the manner of endorsement of renewals thereof;

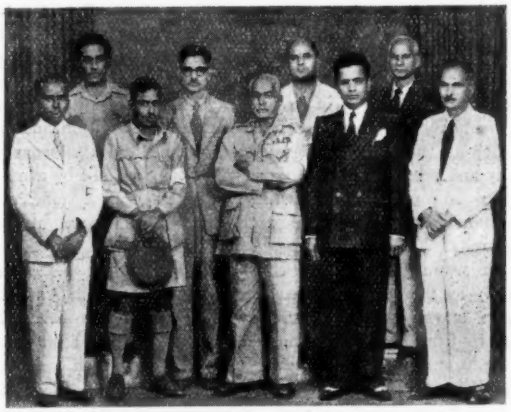
(*k*) the mainteance of a register of students in pharmacy;

(*l*) any other matter which is to be or may be prescribed under Chapters III, IV and V.

NOTES & NEWS

MEDICAL MISSION TO MALAYA

In pursuance of Col. T. S. Shastry's resolution which was passed unanimously by the Madras Branch, the Andhra Provincial Branch, by the South Indian Provincial Medical Conference and by the Working Committee of the Indian Medical Association during 1945 and to implement that resolution Col. Shastry accepted the offer of the Government of India to lead the Medical Relief Parties and to recruit personnel for them. Col. Shastry's recruitment is complete as per personnel below:



Left to right—Dr. N. Janakiram, Major A. Devasahayam, Capt. Y. S. Sastry, Dr. S. Sriama Rao, Lt.-Col. T. S. Shastry (Director). Dr. S. Venkataswamy, Dr. E. A. Shankar, Dr. Tfl Chidanandam, Dr. S. Hanumantha Rao.

Doctors: 1. Dr. S. Hanumantha Rao, L.M. & S., Masulipatam. 2. Dr. E. A. Shankar, M.B.B.S., Malabar (Ex-Malaya). 3. Major A. Devasahayam, L.M.P., Trichinopoly (Ex-Malaya). 4. Dr. S. Srirama Rao, L.M.P., Ellore. 5. Dr. T. Chidanandam, L.M.P., Guntur. 6. Capt. Y. S. Sastry, L.M.P., Vizagapatam. 7. Subadar-Major S. Venkataswamy, L.M.P., Tanuku. 8. Dr. N. Janakiram, D.M.S., Madras.

Male Nurses: 1. M. K. Kapil, Stanley Hospital, Madras. 2. J. D. Jayaraj, Government General Hospital, Madras. 3. M. Jaganathan, Government General Hospital, Madras. 4. V. K. Dhanakoti, Stanley Hospital, Madras. 5. A. C. Samuel, Stanley Hospital, Madras.

Compounders: 1. K. S. Duraiswami, Chidambaram. 2. M. Hanumantha Rao, Repalle, Guntur District. 3. V. Rama Brahman, Manikonda, Kistna District.

Clerk 1: Mr. A. J. Victor, Surgeon-General's Office, Madras.

All equipments were supplied by the Government of India through their Medical Stores approximately costing about one lakh of rupees. Col. T. S. Shastry has been able to secure some fresh clothing owing to the munificence and immediate response of Messrs. Binny & Co. Ltd., and "used clothing" which has been gathered after great labour by the Madras Civic Association. These bales are with the Indian Red Cross, packed and ready for being sent out to Malaya as Red Cross gifts. Col. Shastry expects some amounts of nutrient foods, vitamin tablets, tamarind, dry chillies, etc. from merchants to whom he appealed in the Press and on the platform.

It can truly be said that this Mission of help designated "Government of India's Medical Relief Parties, Malaya" has received the fullest cooperation and sympathy of every grade of society from the Governor's wife and Mahatma Gandhi down to departmental heads and civic workers and the whole of the medical profession.

I.M.A., WORKING COMMITTEE, 1945-46

The Working Committee of the Indian Medical Association for 1945-46 has been constituted as follows:—,

1. Dr. R. A. Amesur, Karachi, President. 2. Dr. Jivraj N. Mehta, Bombay, President of the past year. 3. Capt. P. B. Mukerji, Calcutta, Hony. General Secretary. 4. Dr. K. S. Ray, Calcutta, Editor, Journal of the Indian Medical Association. 5. Dr. R. C. Sen, Calcutta, Hony. Treasurer. 6. Dr. T. J. Lalvani, Karachi. 7. Dr. Ishwardas Bhatia, Amritsar. 8. Dr. A. K. Sen, Calcutta. 9. Dr. P. Gurumurti, Rajamundry. 10. Dr. B. V. Mullay, Sholapur. 11. Dr. M. Motiur Rahman, Jehanabad.

DRUGS CONTROL ORDER

In exercise of the powers conferred by clause 7 of the Drugs Control Order, 1943, read with notification no. E-6246(1)/C.S.-B—E-90-1944, dated January 9, 1945, the Secretary, Civil Supplies Department, makes the following further amendment in the conditions for retail licensee under the said Order and with reference to rule 119(1) of the Defence of India Rules direct that notice of this order shall be given publication of the same in the official *Gazette* of the United Provinces and by supplying a cpoy of the same to the retail licensees in each district.

For condition no. 4 of the said conditions, *substitute* the following:—

"The licensee shall not sell any of the following drugs except on the prescription of a registered medical practitioner: (1) Chloral Hydrate, and (2) Emetine."

* * * *

No. 1-D.M. (1)/A/46.—In exercise of the powers conferred by sub-rule (2) of rule 81 of the Defence of India Rules, the Central Government is pleased to direct that the following amendments shall be made in the Drugs Control Order, 1945, and to direct with reference to sub-rule (1) of Defence of India Rules directs that notice of this order shall be given by the publication of the same in the Gazette of India and by the issue of a Press Note explaining the amendments:—

In clause 5 of the said Order:—

1. In sub-clause (1) after the word "who" the words "is not a Registered Medical Practitioner or who" shall be inserted.

2. In clause (*i*) of sub-clause (2) after the word and letter "Form B" the words "or who is not a Registered Medical Practitioner" shall be inserted.

* * * *

No. 25-D.M.(6)/45.—In exercise of the powers conferred by Cl. 20 of the Drugs Control Order, 1945, the Central Government is pleased to exempt any person appointed by any Provincial Government or any officer thereof to sell quinine substitutes (*i.e.* Mepacrine Hydrochloride and Quinacrine Hydrochloride) on behalf of Government from the provisions of Clause 4, 5 and 14 of the said Order in respect of their purchasing or selling the said Drugs.

THE SIXTH ALL-INDIA PHARMACEUTICAL CONFERENCE, BANGALORE

The following is the summary of Chairman's Address on "The Ideal Course in Pharmaceutics" by Dr. B. Mukerji, D.SC., M.D., F.N.I., Director, Bio-chemical Standardization Laboratory, Government of India, Calcutta, on 5-1-1946.

What is Pharmacy?—The first principle in any planning is to define our objectives clearly, and as far as I can see, this has not been doen in the case of 'pharmacy". Even to-day, there is a considerable amount of loose thinking with regard to the exact 'province' of pharmacy. In many circles, there is still lingering the idea that a 'pharmacist' is nothing but a glorified 'compounder', commonly seen in the dispensing counters of Indian hospitals, in 'dressing rooms' as doctor's assistants, and in many shops commonly designated as 'chemists and druggists' or 'pharmacies'. This conception of pharmacy must be removed once for all before we can proceed to any constructive work.

There is a vast difference between the present-day practice of pharmacy and the functions and duties of 'compounders', as it has been carried on for many generations past in India. Pharmacy, as it is understood to-day, is the science and art of preparing from crude vegetable, animal, and mineral substances and chemicals, medicines in suitable and convenient form for use as drugs, the compounding of drugs, the dispensing of drugs and medicines according to the prescriptions of physicians and their distribution in other ways. With the development of modern medicine and science, the realm of pharmacy has increased considerably. In place of crude preparations and galenicals of unknown strength of earlier days, purified active principles have come into the field. Various synthetic products of the laboratory for defence against disease and infective conditions (chemotherapeutic remedies) have been discovered. The introduction of biological, organo-metallic, endocrine and vitamin products has made a number of new and complex substances available for use in therapeutics, and this list is increasing with rapid strides almost every day. In order to practise modern pharmacy in all its branches, therefore, it is no longer possible to carry on with the limited training of the past given to the 'compounders'. Pharmacy of to-day is an 'applied science' of great significance to medical and public health practice and anybody taking up pharmacy as his career must equip himself with a knowledge of the physical, chemical and biological sciences in such a manner that he can discharge his responsibilities as compounders and purveyors of potent medicaments, narcotics, etc., to the public. Pharmacy has grown to be a borderline science between physico-chemical and biological sciences and as pharmacists training should necessarily be such that he can borrow freely and intelligently from both chemical and biological sciences pertaining to his field of activity.

Guiding principles in formulating a model pharmaceutical syllabus for India—Once this fundamental concept of the comprehensive scope of modern pharmacy is accepted, we can safely proceed to the planning of a model course of study. In making this effort, it would be wise for us to keep three things in view—(*i*) the syllabus must be uniform all over India, (*ii*) the syllabus must recognise the peculiar conditions and status of pharmacy existing in India to-day and must not aim an 'ideal' which would be impossible to attain under the present conditions and (*iii*) the syllabus must be framed taking full advantage of the experience in this direction already available in Great Britain and America.

With regard to uniformity, there cannot be any two opinion that the time has come when an uniform standard of education should be enjoined all over India. At present, a lower grade of training designated as the 'compoundership course' is being imparted in various parts of British India under the auspices of the Provincial State Medical Faculties, or other corporate bodies, not of an University calibre. A Degree course of training is conducted in 4 or 5 Universities (Benares, Andhra, Madras, Bombay, and the Punjab(?)) either independently or jointly with a technology course or applied chemistry course. The courses of study either for the "compounders" or for the 'Graduates' in any two provinces do not agree, with the result that there is no way whatsoever of assessment of values of the qualified pharmacists coming out of the various centres of learning. This practice is certainly not conducive to progressive pharmaceutical education and the creation of an 'All-India profession' imbued with a sense of dgnity and prestige, and therefore should be replaced by a more or less 'uniform' course of study. Pharmacy is a sufficiently important subject to have a Faculty of its own in any University.

In framing the 'ideal' course we should not be guided entirely by the very advanced course now existing in America. I have known of enthusiastic educationists in this field who want to transplant in Indian soil *in toto* the most advanced course of study recommended in some of the Western countries. I am however inclined to be more orthodox in this direction. As a biologist, I believe that for optimum growth, a seedling must adapt itself to the soil and its environment. If we try to usher in even the best course of study in pharmaceutics from abroad, it may not be found suitable to the Indian soil in its present stage of development. The status and pay of the 'compounders', who represent pharmacy in India to-day, is so low that there is a likelihood of a violent shaking of the whole order resulting in difficulties of employments, if suddenly the high standard of American or British pharmaceutical education is superimposed here. We must proceed slowly and cautiously with a forward outlook. We must frame the syllabus in such a way that it can cater both for a lower group of pharmacists and the graduate pharmacists. The practice of pharmacy can be roughly separated into its practice in retail pharmacies and in hospitals and manufacturing concerns. In theory, and probably to some extent in practice, the same standard of scientific training is not needed in both branches. It would, therefore, be desirable to have a dual system of training: (*a*) one catering for the Diploma course in pharmacy and (*b*) the other for the Degree course in pharmacy. The Diploma holders should always have their doors open for the higher degree course any time that they desire to aspire for it. With the progress of pharmaceutical education the two courses may be merged and made into one course later as has been done in America.

In the Report of the College of Pharmacy Committee of the Government of Bengal (1938-39), and later before the Health Survey and Development Committee of the Government of India, 1945, the writer, along with many other experts, have suggested a broad outline of a curriculum for a 'Licentiate course' in pharmacy and a 'Degree course' in pharmacy, which, according to him, would be found suitable to the requirements of India at the present stage. This course is being presented here in a skeleton form for your consideration:

Broad outline of Licentiate course:—

(*a*) The initial standard should be matriculation or equivalent examination with science subjects an essential inclusion.

(*b*) An apprenticeship of 6 months under a person registered with the provincial pharmaceutical council on premises also registered with the council. This apprenticeship must be officially recorded by the council.

(*c*) A two year course at an educational institution approved by the Provincial council.

The following subjects should be studied:—Chemistry, biology, elementary physics, pharmacy, pharmacognosy, elementary pharmaceutical chemistry, elementary physiology and pharmacology and forensic pharmacy.

Examination should be held at the end of the first year and at the end of the course.

The standard of the examination paper should be controlled by the Central Pharmaceutical Council and should be the same throughout India.

The Diploma referred to in the above shall be granted by the Central Pharmaceutical Council and its possession shall be the statutory requirement to enable a person to be a practising pharmacist.

The title of 'pharmacist' should be confined to persons holding this diploma.

Board outline of Degree course:—

The degree should be termed B.Sc. (Pharmacy) or B. Pharm. at the discretion of the university concerned. The subjects studied should be—:

(*i*) Intermediate science including chemistry and physics.

(*ii*) Three years including (*c*) inorganic, organic and physical chemistry, biology, elementary physiology and pharmacology, pharmacy, pharmacognosy, pharmaceutical chemistry and forensic pharmacy.

The holders of the above degree should be made eligible to possess the statutory 'Diploma' without further examination providing they undergo an apprenticeship of one year under conditions similar to those specified in appendix 1.

In order to enable you to examine it critically in the light of the most modern development in this field, I would like you to consider the tentative syllabus (5th edition) outlining the course of instruction for the Degree of Bachelor of Science in Pharmacy (B.S. Pharm.), which has been prepared at a joint meeting held between the American Council of Pharmaceutical Education and the Pharmaceutical Syllabus Committee in Detroit in 1941, and published in 1942. The trend of opinion in America at the present time is that the minimum course of study that would entitle anybody to practise pharmacy should be of four years duration after High School Examination. They do not consider that a lower standard of education of the type of a 'Licentiate', as is being recommended in India and as is still in force in Great Britain, should be encouraged. Such a standard of education, according to American pharmaceutical educators, would not make a person qualified enough to discharge the responsibilities associated with the handling of drugs, poisons and complex chemicals, which are being employed increasing proportions in modern medicine and pharmacy.

In India, however, it would perhaps not be proper for us to aim at such a high standard, at the very outset. However, in trying to prepare the 'ideal' pharmaceutical curriculum, it may be worth while considering the international trends in this field along with the views of some Indian experts, as represented in the skeleton syllabus already presented above. In the latest American curriculum, that has been placed before you, the most striking feature is the large amount of freedom which it allows students in the choice of subjects, particularly during their third and fourth college years. A similar freedom of choice is favoured by many British teachers. Many of the topics included in the American degree as 'optional' subjects, *e.g.*, insecticides, perfumes, and cosmetics, pharmaceutical economics, etc., would form suitable topics for post-graduate courses or lectures to our advanced students. The reason which has led me to point your attention to this syllabus is that it is one of the most balanced curriculum that I have come across. The material to be studied in each subject is given in great detail in the case of both theoretical and laboratory instructions. The details are again divided into work which is 'required' and work which is 'optional'. Apart from the choice of optional subjects, much in the 'required' subjects is left to the discretion of individual colleges.

A word of advice—The present time seems to be most opportune for bringing about a drastic change in our system of pharmaceutical education all over India. Sporadic attempts have been made in many Provinces for the improvement of pharmaceutical education according to their own ideas. This undoubtedly has prepared the ground for a full-fledged pharmaceutical profession of the future, but unless an *uniformity* is brought about, pharmaceutical practice would not come upto any high level of efficiency. The long-sought for all-India Pharmacy Bill which aims at regulating the profession of pharmacy has recently been published (*Gaz. of India*, Dec. 8, 1945). As the Bill has no political bearing, there is every possibility that it will be taken up as one of the first items of business in the Assembly and will soon be put into the Statute Book. Under this Bill, an organized professional body known as the 'Central Council' and 'Provincial Councils' of Pharmacy would be constituted and it is hoped that these bodies would be able to formulate some schemes by which not only an adequate control over the training and examination of those desirous of entering the profession of pharmacy would be possible, but also the registration and licensing of all qualified pharmacists and all establishments where pharmaceutical business of any description is conducted, would be exercised.

DOCTOR-MADE

Hill and Dewar (*Lancet*, **2**:161, 1945) returned to the subject of "effort syndrome," which attracted much interest in the earlier years of the war, but has been less heard of lately. They pointed out again how the symptoms differ from those of organic heart disease.

The patient, however, cannot discriminate. To him breathlessness, precordial pain, faintness, and exhaustion are symptoms of a weak heart, and the heart is a vital organ. In a third to half of the cases the patient has been told by a doctor that his heart was abnormal. Valvular disease has been diagnosed, or the equally ominous term "strained heart" has been used; rest in bed for periods of months has been ordered, games have been interdicted, or light work has been advised in place of heavy work. In these cases a doctor has planted the seed of the anxiety neurosis. That the soil was susceptible does not mitigate the fault. Effort syndrome is in large degree a doctor-made disease. This conclusion is entirely in line with that reached by Paul Wood, who approached the study of the syndrome from the standpoint of an organic cardiologist, entirely free from any psychological bias. The neurosis

grows best and its results are most striking in soldiers, who are forced into a strenuous occupation not of their own choosing, but minor and even major degrees of it are common enough in civilians. Doctors should never offer a diagnosis of heart disease in a young person, explicit or implicit, except on sure grounds. In cases of doubt specialist investigation and advice may sometimes be desirable, but a firm decision should be taken with the minimum of delay. Any murmurs other than the diastolic whiff of aortic incompetence and the rough mitral diastolic or presystolic murmur of mitral stenosis are better disregarded. Much greater harm is done by the mistake of suggesting heart disease or restricting exercise in a patient whose heart is sound, than by allowing activity in one who has a valve lesion. After all, when organic disease is present, nature imposes her own restrictions. Where the diagnosis is doubtful the organ damage cannot be great. The counsel of safety is: exert yourself as much as you comofortably can. The only contra-indication is the continued presence of active rheumatism, as shown by tachycardia, fever, or raised sedmentation-rate after an attack of frank rheumatic fever, and even there the prescription of absolute rest in the later stages is based as much on assumption as on proof of its value.

Effort syndrome is not the only doctor-made disease. Essential hypertension is so easily recognised by the sphygmomanometer that it is revealed in many patients in the early years of its course, when it is producing no symptoms at all, or only minimal symptoms. To inform the patient of it at that stage is often to excite a state of anxiety that itself creates or exaggerates symptoms. This is the price to be paid for any treatment, or any serious alteration in the patient's way of life that may be imposed at that stage. Only the most phlegmatic of middle-aged people can accept without a qualm a diagnosis of high blood-pressure, or a restriction of normal activity, that forecasts an expected shortening of their span of life. The price would be justified if treatment could radically alter the course of the disease. In our present state of knowledge it cannot, and with few exceptions the less a man knows about his blood pressure the better. The gastric field is another where the doctor's preoccupation with the local disease and its treatment may make him under-estimate the effect of his procedures on the patient's mind. Peptic ulcer is known and feared by the laity as a cause of incapacity and sometimes of fatal complications. The diagnosis of duodenal ulcer may be accepted lightly by some but is itself a source of continuing anxiety to many. It is seldom coupled with assurance that ulcers can and do heal, and that complications can usually be successfully dealt with; more often the need for permanent dieting is stressed or the patient's suggestion that his work is physically too strenuous is accepted and acted on. So the anxiety is reinforced. In gastric disorders which come short of actual ulceration army experience has shown that even hospital investigation and the ritual of barium meal examination fix the susceptible soldier's attention increasingly on his stomach and help to perpetuate "functional" symptoms. How far the increased incidence of peptic ulceration between the wars may have been doctor-made is an uncertain but a disturbing question. And how many other doctor-made complaints may be lurking unrecognised among the consulting-room clientele?

The danger of proffering a diagnosis which arouses more apprehension than can be offset by the benefits of treatment is no new thing, but it increases as the lay knowledge of disease and prognosis grows. It becomes more and more important that the doctor should find out carefully just what the patient thinks about his affliction and its implications, and "handle" him accordingly. The danger of over-investigation is of somewhat recent origin. It is likely to grow in an organised medical service, and in an insured population entitled to benefit and compensation. Army doctors who would prefer to act on their clinical judgment alone are sometimes compelled by orders to submit doubtful cases to harmful elaborate investigation in the interest of military efficiency, or to obtain evidence required for pensions decisions; it would have been better in the patient's interest to take a risk and let him carry on. Similar considerations may soon bulk large in civilian practice. The only safeguard lies in having a body of general practitioners who can be trusted and who are trusted. They must have sound knowledge and sure judgment, reinforced by study as well as by experience, and they must be under no direct or indirect compulsion to submit patients to investigations which may do more harm than good. What was recently written of propaganda in relation to health is equally true of ill-judged diagnostic information and ill-judged elaborate examination: "it may aggravate the anxiety of the naturally fearful person, and interfere with the health of the body through the autonomic nervous system. While some people need frightening into taking more care of their health, there are others who would do well to live more dangerously, and many could even afford to let their children do the same!"—*Lancet.*

A NEW REMEDY FOR LEPROSY

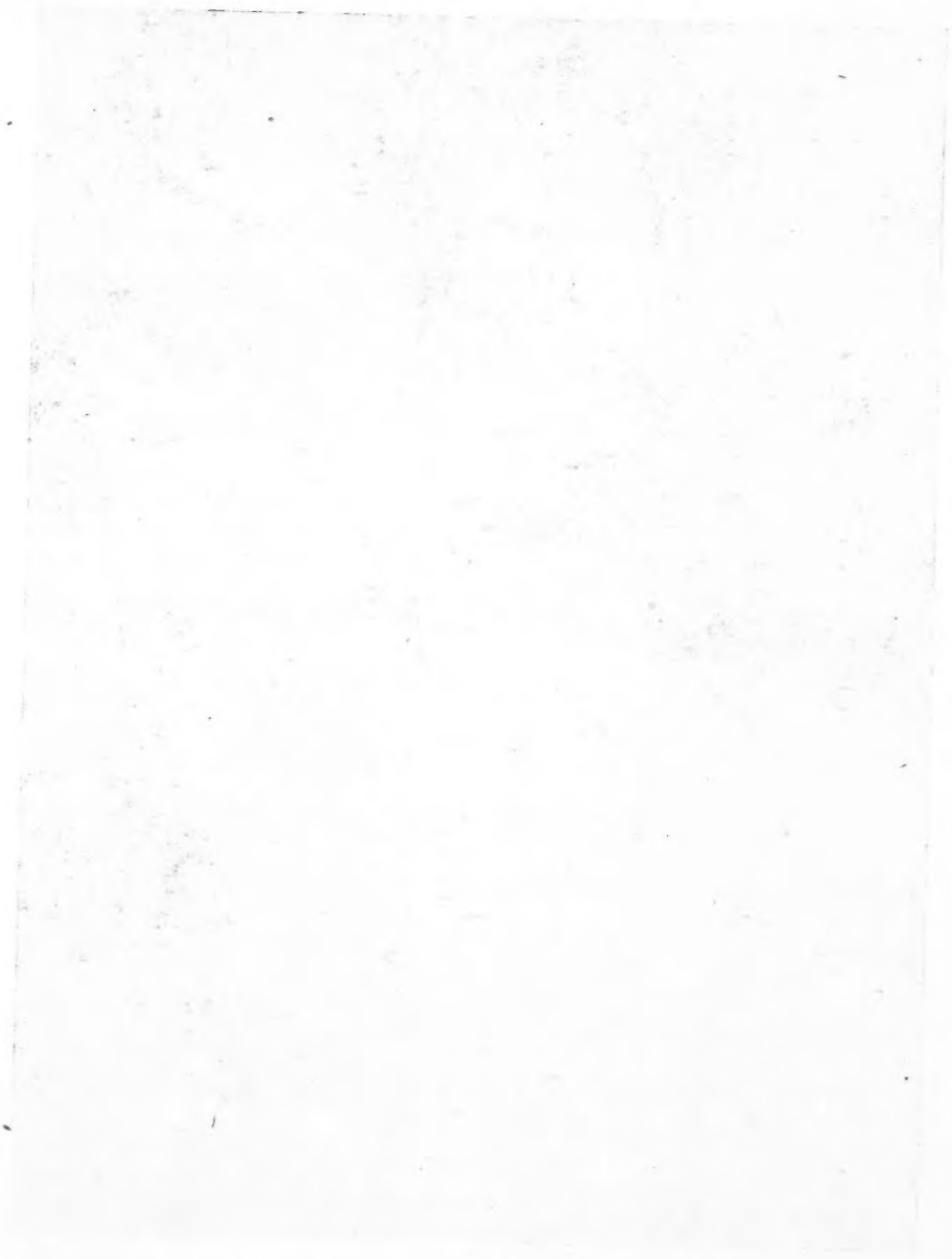
The *British Medical Journal* has received, through the courtesy of the French embassy in London, a copy of a despatch from the colony of Madagascar giving a preliminary account of the discovery of a new remedy which has given remarkable results in the treatment of advanced lepromatous cases of leprosy. In 1937 two French physicians Drs. Boiteau and Grimes, extracted a new glucoside from an umbeliferous plant growing in Madagascar called Hydrocotyle asiatica, which in doses near a toxic level gave encouraging results in leprosy. In 1938, Bonbemps, working in the leprosy laboratory at Antananarivo, the capital of Madagascar, discovered a new glucoside, which he called asiaticocide and which was much less toxic. By further research Boiteau obtained a solution suitable for injection, which he holds, acts as a solvent of the waxy coating of the bacillus of leprosy, which then becomes fragile and can be easily destroyed by the tissues or by an adjuvant drug. In this connection it may be recalled that a British investigator, Leonard Rogers, in 1923 described a defatting action of injections of chaulmoogrates and morrhuates on the bacilli of leprosy and tuberculosis, based on estimates of the lipase in the blood before and after treatment. The results now reported from the new glucoside softening and breaking down of nodules, followed by cicatrization. Healing of whitlows and perforating ulcers and gradual improvement of anæsthesia and muscular atrophy are also claimed. Still more remarkable is the claim that eye lesions are rapidly cured if treated before the posterior chamber is involved.—*J. A. M. A.*

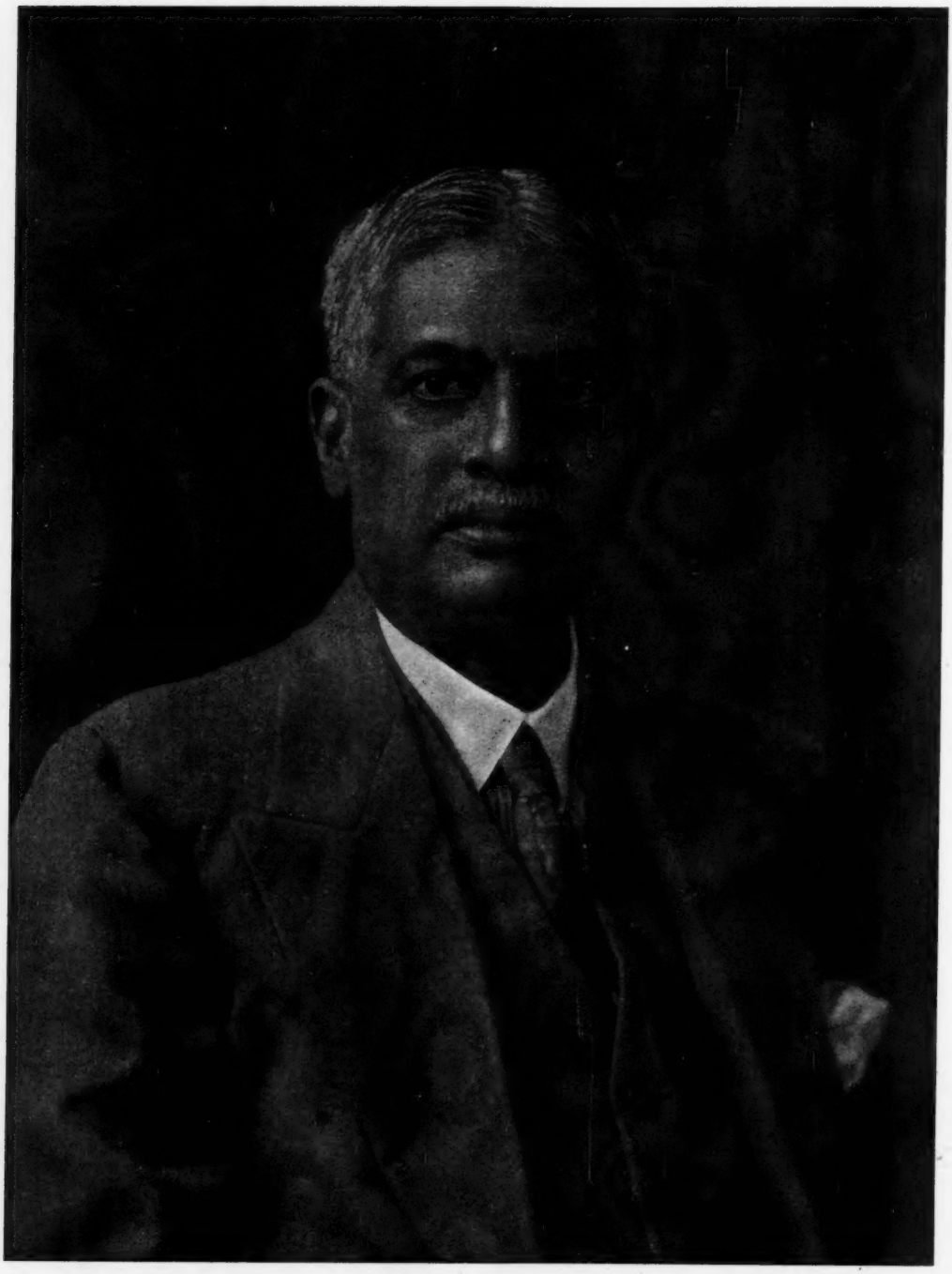
VELLORE CHRISTIAN MEDICAL COLLEGE

The following is the extract of an account of the Vellore Christian Medical College, published in *J. Christian M. A.*, Jan. 1946.

"Sir A. Lakshmanaswamy Mudaliar, Vice-Chancellor of the University of Madras, visited Vellore Medical College on

(*Continued at foot of col. 2, page 2069*





Sir Upendranath Brahmachari, Kt., M.A., M.D., Ph.D., F.A.S.B., F.N.I. etc.
June 7, 1875—February 6, 1946

OBITUARY

SIR U. N. BRAHMACHARI, KT., M.A., M.D., PH.D., F.A.S.B., F.S.M.F., F.N.I.

By the death of Sir Upendranath Brahmachari, India loses one of her foremost medical men, whose work was known all over the World. He is best known for his great discovery of "UREA STIBAMINE" which saved millions of human lives both in India and abroad. This discovery, which was made in 1920 was the result of years of patient chemotherapeutical work, in which he was guided by the pioneer work of Ehrlich. Dr. Brahmachari, besides being a very successful medical man, was also a great chemist, and these two combinations along with his indefatiguable industry and patience were responsible for the discovery.

Sir Upendranath Brahmachari was born on 7th June, 1875, in Jamalpur, E. I. Ry. (Dt. Monghyr), where his father, the late Dr. Nilmony Brahmachari spent the whole of his official career in the Medical Service of the Railway, being held in great esteem by both Europeans and Indians.

Sir Upendranath took his B.A. degree from the Hooghly College in 1839 where he was awarded the Thwyatos Medal for standing first in Honours in Mathematics. He decided to study medicine with higher chemistry. The combination of the knowledge of higher chemistry with medicine no doubt helped him in his future researches. During the course of his studies in the first year, he took his Master's Degree in Chemistry in 1894 from the Presidency College, Calcutta, in the first class, obtaining the University Medal. He passed the M.B. examination in 1898 standing first in Medicine and Surgery for which he obtained the Goodeve and McLeod's medals. He passed the M.D. examination in 1902 and obtained the Ph.D. degree in Physiology in 1904 by his researches on "Haemolysis".

Sir Upendranath entered the Provincial Medical Service in 1898. His versatile knowledge and intelligence attracted the attention of the professors of the Medical College of Bengal. For a short time he worked under Sir Gerald Bomford. He was very soon appointed as Teacher of Pathology and Materia Medica in the Dacca Medical School. In Dacca he did researches with Sir Neil Campbell, Superintendent of the Medical School. Subsequently, he was appointed a Lecturer in Medicine in the Campbell Medical School, Calcutta. This post he occupied for nearly 20 years. He carried on most of his researches in Kala-azar in the Campbell Medical School and it was here that he made his monumental discovery of "Urea Stibamine". He retired from the Government service in 1927 as a Physician in the Medical College Hospitals of Bengal. He was for sometime financed for his researches by the Indian Research Fund Association. Since retiring he had been carrying on researches in diseases such as, kala-azar, malaria, the chemistry and pharmacology of quinoline compounds, and other subjects.

Sir Upendranath won for himself an international reputation as a reasearch worker. Early in his official career, he discovered in 1901 the prevalence of *quartan fever* in Bengal which was considered in those days to be extremely rare in India.

In the course of his researches he drew attention to the remarkable undiscovered skin manifestation of the infection with *Leishmania Donovani*, which was named by him "dermal leishmanoid", a new tropical disease and which had been previously mistaken for leprosy.

Speaking on Urea Stibamine (1929), Sir Upendranath observed as follows in his Presidential Address at the Royal Asiatic Society of Bengal:—

"I recall with joy that memorable night in the Calcutta Campbell Hospital at Sealdah where after a very hard day's work I found at about 10 o'clock in a little room with a smoky dimly burning lantern that the results of my experiments were up to my expectations. But I did not know then that Providence had put into my hands a wondrous thing and that this little thing would save the lives of millions of my fellowmen. I shall never forget that room where Urea Stibamine was discovered. The room where I had to labour for months without a gas point or a water tap and where I had to remain contented with an old kerosene lamp for my work at night, the room still remains but the signs of a laboratory in it have completely disappeared. To me it will ever remain a place of pilgrimage where the first light of Urea Stibamine dawned upon my mind. To-day Urea Stibamine stands prominent in the treatment of Kala-azar in India and as a powerful prophylactic against the disease and it is a matter of supreme satisfaction to me that the treatment evolved out of my research has removed the terrors of this distressing disease. It may be hoped that before long the disease will be completely banished from India and other parts of the world where it occurs—that will be the happiest and proudest day of my life if it falls to my lot to see it".

The Kala-azar Commission, India, used throughout the seven years of their existence Urea Stibamine only, in the routine treatment of kala-azar. *It is no exaggeration to say that approximately 3·25 lacs of valuable lives have been saved to the Province*

Such a great service to humanity, as the stamping out of kala-azar resulting in the saving of millions of life, could not long remain unrecognised. Soon honours from the Government and public bodies began to shower on the discoverer.

The Minto Medal: In making this award, the Director of the Calcutta School of Tropical Medicine and Hygiene made the following remarks: "Dr. U. N. Brahmachari is awarded the medal for 1921. He has made many valuable contributions to our knowledge on malaria, kala-azar and other subjects. His work in connection with kala-azar is well known throughout the world".

The Kaisar-i-Hind Gold Medal: In making this award, His Excellency Lord Lytton, Governor of Bengal, stated: "Your research work in kala-azar has been of the utmost value not only to this province, but to India generally, and the treatment which you evolved through that work has deprived the disease of its terrors. I congratulate you on your achievements and this further recognition which His Majesty the King Emperor has been pleased to give to your humane work".

Knighthood: The following points were noted at Dr. Brahmachari's investure of Knighthood by His Excellency the Viceroy: "Dr. Brahmachari has been President of the Royal Asiatic Society of Bengal for three terms: has done extensive research in connection with tropical diseases such as, malaria, black-water fever, etc., and as a research worker enjoys international reputation; recognised as the leading expert on kala-azar in particular, in the treatment of which he has achieved remarkable success with his 'Urea Stibamine' which he

discovered; has earned a name for philanthropy; is one of the most eminent physicians in Calcutta and is held in esteem also by laymen of all communities.

The Sir William Jones Medal by the Asiatic Society of Bengal was awarded to Sir Upendranath for his researches in kala-azar and other tropical diseases.

He at one time or other occupied the following posts:—

Professor of Tropical Medicine, Carmichael Medical College, Calcutta. Hony. Professor of Bio-Chemistry, University of Calcutta. Dean of the Faculty of Medicine, Calcutta University (1938). Dean of the Faculty of Science, Calcutta University (1939 & 1940). President, Indian Science Congress, 1936. President, Society of Biological Chemists, India. President, Indian Committee, International Microbiological Congress, Paris. President, Section of Medical Research Indian Science Congress Jubilee Session, 1938. President, Section of Medical & Veterinary Research, Indian Science Congress, 1930. President, Royal Asiatic Society of Bengal, 1928 & 1929. President, Board of Studies in Medicine, Calcutta University. President, Indian Association for the Cultivation of Science, Calcutta. President, Indian Chemical Society; Fellow and Patron of the Indian Chemical Society. Hony Vice-President, Indian Red Cross Society; and Member of the Managing Body of the Indian Red Cross Society. Vice-President, St. John Ambulance Association, Bengal Provincial Centre. Vice-President, Governing Body of the Presidency College, Calcutta, and formerly Vice-President, Indian Institute of Sciences of India. First Indian Chairman, Indian Red Cross Society, Bengal Branch. Organizer and First Chairman of the Blood Transfusion Service, Indian Red Cross Society, Bengal Branch. First Chairman, Board of Industries, Bengal. Vice-Chairman, Board of Trustees, Indian Museum. Member, Sanitary Board, Bengal. Member of the Council of Tropical Medicine and Hygiene, International Congress of Medicine, London, 1913. Fellow of the Calcutta University for over 40 years, since the beginning of the Universities Act, 1904 and Member of the Syndicate, Calcutta University for over 30 years. Fellow of the Royal Society of Medicine, London; Royal Society of Tropical Medicine and Hygiene, London; Royal Asiatic Society of Bengal. Hony. Fellow of the International Faculty of Sciences, London; and Hony. Fellow of the State Medical Faculty of Bengal. Formerly Hony. Assistant Surgeon to the Viceroy and Governor-General of India.

He was the author of:—Studies in Hæmolysis, Calcutta University Press, 1913. Kala-azar in Dr. Carl Mense's Handbuch der Tropenkrankheiten, Vol. IV, 1926. Treatise on Kala-azar, published by John Bale Sons & Danielsson Ltd., London, 1928. Campaign against Kala-azar in India, Jubilee publication on the 80th Birthday of Dr. Prof. Bernhard Nocht Hamburg, 1937. Infantile Biliary Cirrhosis in India, British Encyclopaedia of Medical Practice, Edited by Sir Humphrey Rolleston, 1938. Progress of Medical Research Work in India during the past twenty-five years, Indian Science Congress Association, 1938. Gleanings from my researches, Vols. I and II, Calcutta University Press, 1940, and numerous articles in Indian Journal of Medical Research, Indian Medical Gazette, Journal & Proceedings of the Royal Asiatic Society of Bengal, Journal of the Indian Chemical Society. Bio-Chemical Journal, British Medical Journal, Lancet, Journal of Tropical Medicine & Hygiene, Journal of Pharmacology and Experimental Therapeutics, American Journal of Tropical Medicine, Transactions of the Royal Soceity of Medicine & Hygiene, Indian Journal of Medicine, Calcutta Medical Journal, Transactions of the Far Eastern Association of Tropical Medicine, Comptes Rendus et Congress International de Medicine Tropical et D'Hygiene, Cairo-Egypt (1928) dealing with subjects including chemistry and chemotherapy of organic antimonals, chemistry and chemotherapy of quinoline compounds, kala-azar, dermal leishmanoid, malaria, blackwater fever, haemolysis, anopheles, etc. The number of his publications is more than 150.

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November 22, 1945. His report was submitted to the syndicate of the University and their decision has now been communicated to us. Permission is granted to admit third, fourth and fifth year students from January, 1946. The question of permanent affiliation will be decided after considering the report of a commission which is to visit Vellore in the academic year 1947-48. In December, 1947, Vellore medical students will be taking their final examinations for the M.B., B.S. degree. In January, 1947, there is a possibility that a limited number of L.M.P., and D.M.S. graduates may be re-admitted for a further course of two years leading to the M.B., B.S. degree.

"The most significant development during the past two years, which more than any other single factor has led to the achievement of provisional affiliation, is the splendid co-operation of the Churches in India, North America, Britain and Australia. There are now 39 Mission Boards co-operating in the support of Vellore. This broad basis of denominational co-operation in an educational institution is perhaps unique in the history of missionary enterprise. Other significant developments during the past two years are as follows: 1. The in-patient accommodation has increased from 284 to 414 beds. 2. The daily out-patient attendance has increased from 200 to 500. 3. The staff has more than doubled. 4. A new Pathology, Bacteriology and Hygiene block has been added to the Hospital, and a capital sum of Rs. 5,00,000 has been expended in new buildings and equipment. 5. Annual expenditure has increased from Rs. 2,83,149 in 1943 to Rs. 5,48,048 in 1944-45. 6. Annual income has risen from Rs. 2,83,407 in 1943 to Rs. 4,29,960 in 1944-45.

"The most disturbing feature is the rapid rise of annual expenditure over income. The next five years will be critical. We cannot expect much increase in Hospital Free Income as single bed private wards are being used to accommodate three and four poor patients. We shall practise every reasonable economy, but the fact remains that unless our annual income is increased considerably we cannot go on. Here is a challenge to us all; for this, indeed, is our College. We have chosen Vellore as the centre for an All-India Christian Medical College. It is time to remind ourselves again of the policy to which we are committed when we resolved that 'We state emphatically that we regard Christian Higher Medical Education as the most urgent and most important project for Medical Missions in India—so important that, if it cannot be attained otherwise, some of the medical work in India should be sacrificed even though the loss would be great'."